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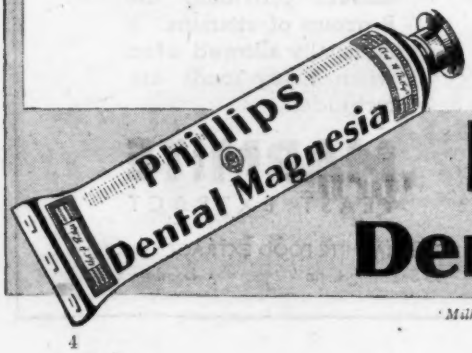

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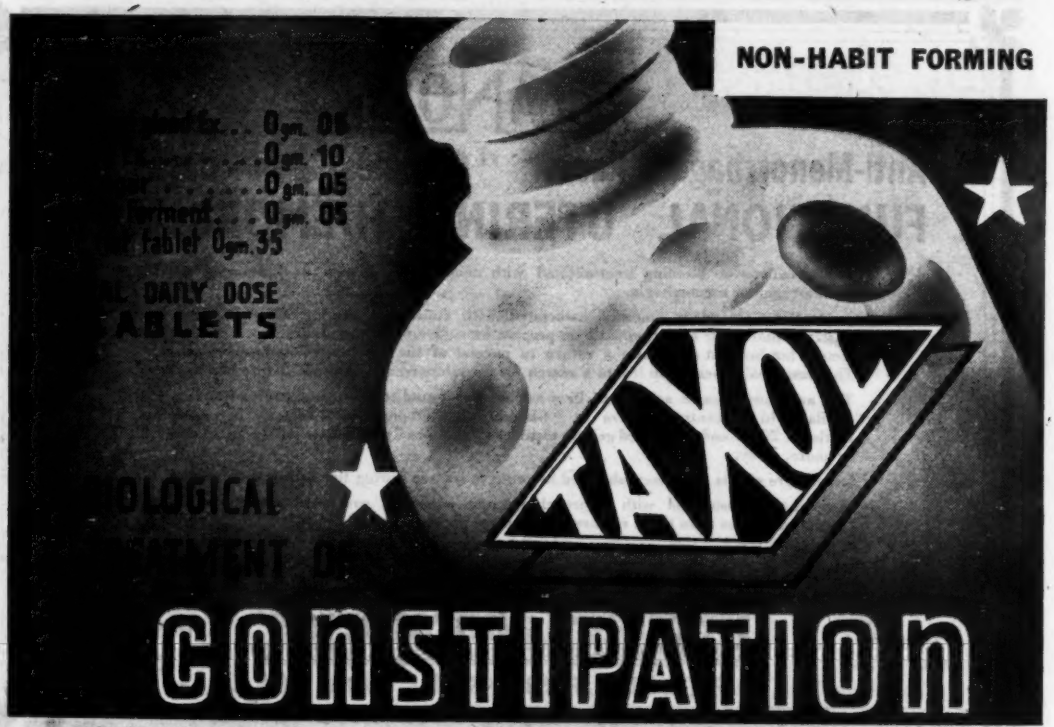

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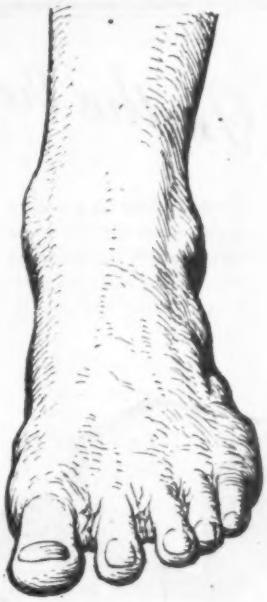

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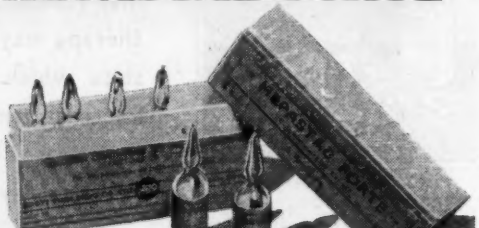

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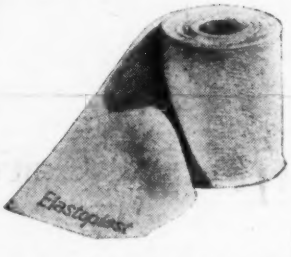

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SHOCK-PRODUCING FACTOR(S) FROM STRIATED MUSCLE

I.—ISOLATION AND BIOLOGICAL PROPERTIES

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IT would be impossible to review here the vast amount of work on experimental shock, even in the last decade, to much of which any worker in this field must be greatly indebted.

Three main theories have held sway: (1) exhaustion of the nervous system, (2) local fluid loss, (3) toxic factors from damaged tissue. This report is concerned with the last hypothesis which first attained prominence following the investigations of H. H. Dale and W. M. Bayliss during the last war and has never since, in spite of opposing theories, lacked considerable support. Evidence is presented that a substance can be extracted from healthy muscle, which, on injection, produces some of the signs and symptoms of shock. It should be emphasised from the outset that it has still to be determined whether this substance is in any way responsible for the shock syndrome caused by any form of tissue trauma.

The observations reported cover a wide range, and as their scope has expanded other workers have helped. Inevitably some findings relevant to the conclusions are omitted from this preliminary report. A confusing feature is the variability of animal response, and such figures as are given represent an approximation to the mean of different experiments.

The work started in an effort to reproduce the crush syndrome experimentally by the method, introduced by Allen (1939), of complete hind-limb ischæmia, produced in this instance by applying metal clamps to the upper thigh(s) in anæsthetised rats, mice, guineapigs and rabbits. The findings suggested that a renewal of the search for the hypothetical muscle shock factor was justified.

The following observations in particular supported the hypothesis.

(1) After complete asphyxia of the rat hind limb for 7 hours, amputation within 2½ hours of release of the clamp might save all the animals. From 2½ hours onwards the survival-rates steadily fell, to reach zero, on the average, at 4 hours. At a time when amputation was unsuccessful, the calculated local fluid loss often appeared insufficient to cause death.

(2) Rat plasma, injected intravenously, did not significantly decrease the mortality-rate, even when given soon after release of the clamp and in repeated doses.

(3) The rapid recovery from sublethal periods of limb asphyxia contrasted greatly with the progressive deterioration always observed after a lethal period. Moreover, if the clamps (in this case on both legs) were released for a short time (e.g., 15 minutes after 2 hours' application) they had to be reapplied for a further period closely approximating to the lethal time (e.g., 4 hours) in order to cause death. The rat could withstand repeated sublethal periods of asphyxia in both legs, totalling at least 12 hours over a 32-hour period. Apparently the destruction or removal of the factor(s) responsible for death was very rapid, and the results suggested that there was a lethal threshold level at its site of action which, once attained, led to irrecoverable systemic changes.

(4) A tolerance could be acquired to the effects of limb asphyxia, so that, for example, rats were "trained" to withstand asphyxia of both hind limbs for 7 hours (cf. lethal time of 3–4 hours in controls) by progressively increasing the asphyxial time at 3-day intervals.

(5) Complete anuria in the non-survivors; or, in the survivors, anuria followed by oliguria, sometimes with red cells, blood pigment, casts or albumin in the urine.

All these facts supported the concept of a toxic factor released from asphyxiated muscle, and observations (1) and (2) suggested that it did more than merely increase local fluid-loss into the tissues.

Search for a Toxic Factor

From this standpoint, attempts were made to obtain a muscle extract which, on intramuscular injection, would reproduce the syndrome produced by limb asphyxia. Preliminary experiments with intraperitoneal implantations of minced rat muscle, mixed with sulphathiazole, were negative except in showing that the sulphonamide prevented infection. Among others the following methods, using rats, were tried, mainly without success, though toxic effects were observed erratically.

(1) Saline extracts of rat muscle frozen with CO_2. Injections were made into normal rats and into rats in which the hind limbs had been clamped for a sublethal time, with the idea that the extract might contain a factor which could supplement or complement the hypothetical factor coming from the damaged muscle.

(2) Similar extracts from asphyxiated limbs before, and at various periods after, release of the pressure.

(3) Similar extracts from limbs which had been warmed or cooled during the period of asphyxia.

The time between death and extraction of the muscle was very variable, and the question arose whether the hypothetical shock factor was very labile and perhaps rapidly destroyed in the dying muscle. Acting on this hypothesis, rabbit muscle was minced into boiling saline immediately after removal. This crude extract was consistently more toxic than any previously used, though there was no obvious difference in those prepared from asphyxiated or from normal muscle. Nevertheless, the idea of an unstable toxic factor in muscle had received some support, and a search was made in the literature for any further clue. A possible link was found in two short papers by Dyckerhoff et al. (1939).

They sought to find whether Lenggenhager's (1935–37) contention was true, that the rapid lethal effect of a fresh rabbit muscle extract given intravenously in the rabbit was due to intravascular clotting produced by thrombin. Dyckerhoff found no thrombin in the extracts but large amounts of thrombokinase. The extract lost its lethal potency completely after 2 hours' standing, but not its thrombokinase, which increased. After removing the thrombokinase from fresh muscle with acetone, saline extracts still killed the rabbit on intravenous injection, but larger amounts were required; the original lethal potency was restored by adding thrombokinase in the form of old muscle extract. It was concluded that the lethal effect was due to two factors, "myotoxin" and thrombokinase which, in combination, produced collapse with extensive thrombosis. The muscle extract was purified by a two-stage alcoholic precipitation with the production of a water-soluble powder.

Apart from a description of the rapid lethal action in the rabbit, no biological observations were reported, possibly because the main object of the work had been achieved.

It was to be expected that the effect described by these workers was non-specific and closely related to that produced by the intravenous injection of many tissue extracts. Nevertheless, this demonstration of an unstable lethal substance in muscle suggested, in the light of our earlier findings, that such an extract might produce more chronic effects if given by routes other than the intravenous. This proved to be so.

Many early experiments were made with the crude saline extract (My_A). All the observations have been confirmed with the more purified fraction (My_C) named myotoxin by Dyckerhoff, or with modifications or still more advanced fractions of this (Bielschowsky and Green 1943). The factor or factors producing a shock-like state after intraperitoneal, intramuscular or subcutaneous injection was provisionally called MSF [Muscle Shock Factor(s)].

CONSEQUENCES OF INJECTING MSF

Intravenous injection.—It was easy to confirm the rapid lethal effect on intravenous injections in the rabbit and also to demonstrate a similar acute effect, with alternating head-retraction and signs of central nervous irritability in mice and rats. Death is preceded by a period of profound dypsnœa, with stridor and deep forced inspiratory movements at long intervals, culminating in complete respiratory paralysis. A wide variation in the MLD was noted—in part correlated with age, for the young tolerated larger doses than the older animals. Another striking feature was the rapid recovery from a sublethal dose and the ability to withstand repeated sublethal doses at short intervals without causing any permanent harm. This effect resembled the tolerance of the animal to repeated non-lethal periods of limb asphyxia. Direct blood-pressure ob-

servations in the cat and rabbit revealed the presence of a powerful depressor substance whose properties will be considered presently.

Intramuscular injection.—Having confirmed the acute lethal effect, the intra-muscular route was next chosen to find whether the local changes produced would resemble those seen after hind-limb asphyxia. A remarkable similarity was observed. The condition seen in the rat after a lethal dose was briefly as follows:

The rat becomes less lively in a few minutes. There is increasing listlessness, loss of irritability, progressive weakness and rapid shallow respirations followed by marked slowing at a later stage. The thigh becomes progressively swollen. The body temperature falls rapidly and progressively, remaining very low until death. Hæmoconcentration quickly sets in and may increase until death. Towards the end the animal merges into a dead-alive state; the respirations are slow, irregular and laboured, and finally cease at a time when the greatly dilated heart is still beating slowly. Consciousness is not lost until death, and though the animal responds only sluggishly to any environmental or superficial stimuli, it shows a delayed but more pronounced reaction to deep painful stimuli, which is much more striking in the hind-limbs. The blood-pressure (using the ear-occlusion method) shows a gradual fall. Usually no urine is passed except possibly very shortly after the injection. Death occurs in from 2 to 36 hours, the survival period varying directly with the dose and with the particular muscle fraction used. It may be as late as 72 hours, but this late survival cannot be produced regularly, since a lethal dose usually kills within 24 hours, and if the dose is slightly less than lethal the recovery phase is well advanced by this time.

If the animal is killed when moribund, the most consistent findings are: the very low bleeding volume; the viscous dark purple unclotted blood in the heart and main vessels; and the advanced local œdema of the thigh muscles, often with a subcutaneous exudation of what appears to be clotted plasma spreading subcutaneously into the inguinal region and even into the abdominal wall. On section the bulging muscles exude serum, they show scattered pale areas suggesting early necrosis. There are effusions, sometimes very large, of clear, yellow or slightly milky unclotted fluid in the pleural and peritoneal cavities. The lungs are bulky, œdematous and much congested, often with small superficial hæmorrhages, and the right heart is grossly dilated. Other common findings are gross venous congestion in the liver and large veins, and dark digested blood in the small intestine and sometimes in the stomach. All the tissues, including the brain, appear more moist than usual. The kidneys are often slightly enlarged and œdematous and darker in colour; the bladder is empty.

The striking feature after sublethal doses is the rapid recovery, and even with doses closely approaching the lethal, all the more precise findings to be detailed have usually returned to within normal limits in 24 hours. The thigh, however, may not resume its normal girth until the 2nd or 3rd day.

Intraperitoneal injection.—Similar general effects are seen after intraperitoneal injection; the post-mortem findings are similar, except that the exudates are usually larger and sometimes enormous while the peritoneal exudate is often very turbid, partly because of polymorph exudation. The lethal dose is somewhat smaller by this route and distinctly higher by the *subcutaneous* route.

These findings, like many others, suggest that if the concentration of MSF in the blood does not reach a certain level, the changes leading to death are not initiated.

Histological changes.—In general the histological changes in the tissues, except perhaps the kidney, add little information to the gross findings. There are, however, many exceptions to this statement, and an extensive inquiry into the fine morphological changes is required. Meanwhile chief attention has been paid to the kidney.

TEST ANIMALS AND SOURCES OF MSF

MSF produced similar effects in all species tested—rat, mouse, guineapig, rabbit and cat. The effects appear the same in all species, but widely different doses are required to produce them. The rabbit and guineapig are much more susceptible than the mouse and rat, while the cat is the most resistant animal tested. Intraperitoneal injections in mice are chiefly used for routine MLD tests.

Active extracts have been made from the voluntary muscle of the rabbit, ox, guineapig, rat, cat and man: all have very similar biological properties. Ox muscle is at present being used for large-scale production.

The Depressor Factor

The finding of a powerful depressor factor in the muscle extract naturally led to its study in detail; for a fall in blood-pressure (BP) is assumed to be the most important criterion of traumatic shock, and is one of the few features common to all forms of experimental shock.

On injecting the extract intravenously into the anæsthetised cat or rabbit the fall, often preceded by a slight transitory rise, is precipitous and is accompanied by severe bradycardia. This stage is quickly followed by a rise nearly as rapid, covering roughly two-thirds of the fall, and the heart resumes its normal rate. The second stage of recovery is much slower and may be preceded by a slight secondary fall. The rise may proceed to a level somewhat above the starting-point and then slowly return. The effect is quantitative, and with a single large dose the BP can be maintained below normal for as long as 20 minutes, though it is the second stage of recovery which occupies much the larger part of the recovery phase. A fall of BP to a level of a few millimetres is obtained by a dose very much below the lethal, and any further increase in dose only prolongs the recovery phase. With a fatal dose the pressure never recovers, except sometimes for a slight temporary asphyxial rise. The heart-beat becomes slower and more feeble and ceases in 10–20 minutes. Respiration has usually stopped at the outset. If artificial respiration is given before the heart is too feeble, the BP gradually rises, and it has been observed to return to normal and remain there for an hour without any return of spontaneous breathing. The effect in cat and rabbit is very similar, except that the second stage of recovery is longer in the rabbit.

The relations of this depressor factor to other known tissue depressor substances have been studied. It is not histamine, for it has a powerful effect on the rabbit; it is not destroyed by histaminase; it is insoluble in acetone and in 75% alcohol, and it is unstable in acid solution; moreover, striated muscle is a poor source of histamine. It is not acetylcholine, for it is not antagonised by atropine (apart from the bradycardia effect, which is) and its chemical properties are different. It is not kallikrein, for it is not destroyed by boiling; nor is it Gaddum's P factor, for it is not destroyed by boiling in alkaline solution.

Its biological properties strongly suggested adenylic acid or its derivatives. With the active adenine compounds it shares the following effects:

(1) A depressor action not antagonised by atropine.

(2) Dilatation of the peripheral blood-vessels, as indicated by a greatly increased outflow from the perfused cat hind-limb.

(3) Leucocytic reaction in rabbit eye (Bennet & Drury 1931).

(4) Rapid inactivation by muscle and tissue extracts, and by blood.

Its effect on the guineapig heart, though not precisely the same as those described for adenosine or adenylic acid, was compatible with its being a related compound. It was observed to stimulate peristalsis of the stomach and intestine in the intact animal, whereas most of the adenine compounds inhibit it in vitro (Drury 1936). Gillespie (1934) showed, however, that though adenosine triphosphate causes relaxation of the intestine in vitro a stage of increased tone follows.

Detailed comparison with the effects of various adenine compounds on the BP and heart, and consideration of the rapid destruction of its depressor action by a saline muscle extract and by blood, suggested its identity with adenosine triphosphate. This substance has now been isolated in amounts sufficient to account for almost the whole of the depressor activity of the muscle product (Bielschowsky and Green 1943).

Are the Depressor and Shock Factors Distinct?

It was at first thought that the shock-like effect and the killing power of the muscle products given intraperitoneally ran counter to the idea that MSF was identical with one of the biologically active adenine compounds; for these do not appear to be lethal in a comparable dosage (Drury and Szent-Györgyi 1929). Comparative tests of the lethal potencies of substances containing MSF and of adenosine, yeast adenylic acid and cytidylic acid supported this view. Nevertheless, preliminary tests indicate the shock-producing and lethal potencies of adenosine triphosphate are largely, if not wholly, responsible for the described properties of MSF.

In the light of the last statement the problem of a possible distinction between the depressor factor and MSF does not appear very relevant; but it arose for the following reasons.

On the assumption that the depressor factor was an adenine compound the effect of treating the muscle product (Myc) with N HCl was tested. The depressor factor was destroyed partially after 10 minutes' boiling and completely after 30 minutes. (Similar treatment with N NaOH was without effect.) But the acid-treated material retained the larger part (roughly 65%) of its original lethal potency, and a substance having many of its biological properties—except the acute depressor action—could be precipitated from solution with methyl alcohol. Most of the animal responses (see table I) attributed to the action of the MSF were obtained with the muscle products hydrolysed by acid.

There appeared to be other distinguishing points. Though it was easy to destroy the depressor action by incubating the substance with a saline muscle extract, or with fresh whole blood or plasma, the lethal property was not diminished and sometimes seemed to increase. The depressor factor could be almost completely precipitated by treatment with acridine, but the lethal factor appeared to be divided fairly equally between precipitate and filtrate, and a combination of the two restored the MLD to that of the original substance.

Another apparent difference was that sometimes, though not always, the dialysed crude extract (Mya) lost its depressor action but not its killing power. Again, in the rat limb after a period of ischæmia the rates of disappearance of the depressor factor and MSF seemed to differ.

Not all these differences have been fully explained, but there are good reasons for thinking them more apparent than real. Recent observations support the following hypothesis. Adenosine triphosphate is the substance mainly responsible for all the described effects of the muscle products. While, however, the adenosine radicle is the depressor factor and responsible for the "myotoxin" effect—i.e., rapid death after intravenous injection—the pyrophosphate radicle is responsible for some, at any rate, of the more prolonged shock-like effects ascribed to MSF. Tests with inorganic pyrophosphate support this view. Under the conditions of acid hydrolysis used, the adenosine radicle is split up and loses its depressor action, while the pyrophosphate radicle remains in part intact. On the other hand, under the conditions of alkaline hydrolysis used, adenylic acid is formed and the pyrophosphate radicle remains intact; so both the depressor and MSF properties are retained. The rapid destruction of the depressor action by blood and by a saline tissue-extract is of course explained by their richness in the enzyme deaminase.

Effects on Function

HÆMOCONCENTRATION

The concentration of the blood seen after injection of MSF is, like all these responses, very variable. It is never so great if the quantity of fluid injected is large; but, apart from this, it may be absent altogether, very transitory, or at any rate easily missed. In the rat given a lethal dose, the blood hæmoglobin begins to rise in a very short time and in 1–5 hours reaches a maximum, where it may stay until death, particularly when the survival period is only a few hours. The figure reached is not usually above 150% (Haldane) in the rat (normal 110%), and in the mouse it is lower.

In rats surviving for roughly 12–24 hours the hæmoglobin level has often returned to normal, or slightly below, when the animal was moribund. The average figure at death in one group of 21 rats dying within 24 hours was 118%. In a comparable group of rats dying from the effects of ischæmia of both hind limbs, the corresponding figure was 140%. After the latter treatment the rise in hæmoglobin is much more pronounced—up to 210% in the moribund stage. As in the former group, but not so frequently, the figures may drop to normal or subnormal levels before death. The lower figures in the MSF treated rats may be due, in part at least, to the injection of relatively large quantities of water in which the substance is dissolved. With either treatment, a progressive fall in hæmoglobin to well below the normal was observed in a high proportion of rats surviving over 24 hours; it continued over several days, and while figures between 70 and 90% were common, values down to 50% were seen. This is presumed, though not proved, to be an indication of hæmodilution.

Although very many hæmoglobin estimations have been made, their interpretation is complicated by variations in the quantity of fluid ingested. One possibly significant point is that in the state produced by MSF, or by clamping the hind limbs, absence of hæmoconcentration—at least in any one determination—does not necessarily mean absence of "shock" or that the animal will necessarily survive. On the other hand, figures above 150% usually indicate a fatal result.

FALL IN BODY TEMPERATURE

This is a striking and consistent finding. It begins almost immediately after the injection of MSF and the temperature may reach 30° C. (normal is 40° C.) within one hour. It tends to continue progressively downwards until death. A similar immediate effect is seen after the injection of saline, but the fall is in no way comparable and lasts only a few hours.

Rectal temperatures as low as 22° C. have been observed in the living animal and temperatures of 25–30° C. may persist for several hours. Even with sublethal doses temperatures as low as 30° C. are recorded. The fall is a very sensitive index of the presence of MSF in the tissues, and it may prove to be a means of assay, though the individual response is very variable. The fall is no doubt associated with a profound lowering of the basal metabolism, but no precise determinations have yet been made.

The effect resembles that reported by Bennet and Drury (1931) in the guineapig after injection of adenosine. It is, however, observed with muscle extracts (e.g., after acridine precipitation) which do not show the intravenous depressor effect typical of the adenine compounds.

EFFECT ON RESPIRATION

After a lethal dose given intravenously, respiratory movements usually stop and may not start again. Often after a short period there are a few violent inspiratory gasps at irregular intervals before final cessation. With a non-lethal dose there is a short period of apnœa followed by deep laboured stridulous breathing for a few minutes. The period of dyspnœa is followed by one of rapid shallow respirations, a stage which can be observed for an indefinite period in a rabbit given a continuous-drip perfusion with tolerated amounts of the muscle extract.

When MSF is injected into the rat by other routes there is a period of rapid respirations; but the rate gradually diminishes and may fall to around half the normal. Just before death the respirations are irregular and gasping and there is often stridor; when they cease the heart continues to beat slowly for some time. The lungs are usually œdematous, well expanded and sometimes emphysematous at autopsy. The nature of these effects has not been studied in detail (after vagal section for example). They are probably all due to asphyxia of the respiratory centre, though bronchial spasm may play a part. There is also other evidence of asphyxia of the central nervous system in rats after treatment with MSF. Signs of cerebral irritation, in the form of violent convulsive movements of different parts of the body at irregular intervals, are sometimes seen in the moribund stage.

EFFECT ON RENAL FUNCTION

It was early observed that a period of anuria followed the injection, even when large amounts of fluid were

injected at the same time. With a lethal dose this is absolute and the bladder is empty at death. With a sublethal dose the period of anuria may be very long—even up to 72 hours. This period may be followed by diuresis, and in roughly a quarter of the rats pathological changes in the urine were seen, such as albumin, granular casts, a positive benzidine test, occasionally red cells, and rarely frank hæmaturia. These changes closely resemble those seen after limb ischæmia, but except for the anuria which is more prolonged, they are not so severe. Their possible bearing on the "crush syndrome" and traumatic anuria in man, and the fact that the output of urine was easily recordable, and might therefore be used as a method of assay, led us to concentrate our attention on renal function.

The *blood non-protein nitrogen* (NPN) progressively rises in fatal cases, terminal values in the region of 100 mg. per 100 c.cm. (highest observed, 120) are usual. With sublethal doses the rise appears to be transitory, and figures only slightly above normal have been observed 18 hours after the injection, at a time when no urine had yet been passed. This increase in NPN is probably renal and not extrarenal in origin.

Output of urine.—Direct observations on the flow from the exteriorised ureter in the rabbit, after clamping the opposite renal vessels, have been made. After intravenous injection of a small dose of MSF, the flow of urine stops at once, and anuria persists for a period after the BP has returned to normal. This period varies with the amount injected and may be as long as 2 hours; diuretics usually have no immediate effect in overcoming the anuria. The same effect is also seen after destruction of the acute depressor factor by acid hydrolysis, and is therefore not a direct result of diminished glomerular filtration due to a low BP. In the cat anuria coincides with the fall in BP; but the cat is much less sensitive to MSF than is the rabbit.

Pressure in renal artery.—A few observations have been made on the pressure changes in the renal artery of the perfused isolated cat kidney. The effect is complicated, but even with minute doses the main evidence is of renal vasoconstriction. In one instance alternating vasoconstriction and dilatation, with an enormous range, began immediately after the injection and continued throughout the experiment. Oncometer observations on the intact kidney also suggest that vasoconstriction is the predominating effect. It is not yet known whether these reactions occur in the absence of the depressor factor.

Though there is little doubt that renal function is severely modified in the rat, definite evidence of structural changes in the kidney has been difficult to find.

At *autopsy* the kidneys appear darker than usual; they may be enlarged and œdematous. The inner cortical zone often seems more prominent, contrasting in its paleness with the outer zone. Estimations of the water content of a large number of pooled kidneys showed a definite increase (about 5%) over the control group. An almost exactly similar increase was seen in a comparable group of rats dying after limb ischæmia. A dehydration method was used; the results should therefore be confirmed by other methods.

Precise *histological evidence* of kidney damage has been hard to find. The rat kidney undergoes rapid autolysis, and even when it is removed from the healthy living animal direct into fixative, early changes in the cells of the convoluted tubules which would be interpreted as pathological, though presumably physiological, are seen.

Nevertheless, over a large series the definite impression is gained that changes in the lining cells of both the first and second convolutions—especially perhaps the second—are more advanced than in the control animals. These changes consist in loss of the brush border, and swelling, vacuolation and early necrosis or fragmentation of the cell. As would be expected, they also seem to become more obvious as the survival-time increases. Casts of various types, though not numerous, are often seen; they are mainly granular, sometimes cellular or hyaline, and rarely amorphous pigmented bodies. Changes in the glomeruli are irregular and usually absent or mild. Though definite changes have been seen in the capillaries, they are at present too erratic to warrant description.

Various subsidiary treatments designed to modify renal function and thus possibly give clearer histological evidence of renal damage, were undertaken—e.g., diminution of the fluid intake and administration of $Na\ H_2PO_4$. No significant results were obtained.

A greater measure of success was obtained by injection of *myohæmoglobin* * a short time before injecting MFS. This substance (tried only in amounts of 200–500 mg. per kg. body-weight) strongly reinforces the effect of MSF, so that only half, or even less, of the usual lethal dose is fatal. Given alone in the rat it has no obvious effect apart from the fact that oliguria and a rise in the blood NPN are observed. Combined with a dose of MSF insufficient in itself to produce anuria or affect the blood NPN, there is prolonged anuria and a large rise in the NPN (e.g., at 18 hours: MSF alone, 34·6; myohæmoglobin alone, 86·0; MSF + myohæmoglobin 186·1 mg. per 100 c.cm.). In the few kidneys examined, a striking dilatation of the second convoluted and other tubules together with large numbers of amorphous brownish-yellow casts (presumably myohæmoglobin) were seen. In the other groups there were no comparable changes except for a relatively small number of pigmented casts in the myohæmoglobin group.

Comparison of Effects of MSF and Limb Ischæmia

Some of the more important resemblances are summarised in table I. Some of the findings listed there, which have not already been discussed, must now be considered.

TABLE I—COMPARISON OF FINDINGS IN "SHOCK" INDUCED BY INJECTION OF MSF OR BY ISCHÆMIA OF BOTH HIND LIMBS

MSF	LIMB ISCHÆMIA
General signs and symptoms.	Indistinguishable.
Survival time proportional to dose.	Survival time proportional to duration of ischæmia.
Local œdema and exudation.	Similar but more obvious necrosis (at level of clamp).
Early and patchy muscle necrosis after intramuscular injection.	
General autopsy findings.	Similar. Noteworthy absence of gross lesion sufficient to account for death.
Delayed but then progressive fall in blood-pressure.	Gradual fall in blood-pressure remaining low until death.
Gradual fall in respiratory rate and increasing dyspnœa.	Later stages similar with slowing, dyspnœa and failure whilst heart still active.
Fall in body temperature.	Not seen until later stages but then progressive.
Hæmoconcentration often followed by hæmodilution.	Similar. Time relations comparable but final concentration often greater—sometimes extreme; possibly due to additional local fluid loss in inflammatory exudate produced by injury.
Renal dysfunction with rise in NPN, accentuated by myohæmoglobin. Structural changes in kidney slight but very evident in combination with myohæmoglobin.	Similar except that pathological changes in urine more frequent.
Rapid recovery from sublethal doses.	Rapid recovery from sublethal periods of ischæmia.
Acquired tolerance to increasing doses.	Increased tolerance to longer periods of ischæmia.
†Cumulative lethal effect of ½ MLD	+ ½ lethal ischæmic time.
†Tolerance much diminished after hæmorrhage or operative procedures.	Tolerance much diminished after hæmorrhage. Effect of other forms of tissue trauma not known.
†Late deaths up to several weeks possibly due to lowered resistance to infection.	Similar.

† Indicates that tests were not made with material free from the depressor factor.

One of the most important perhaps is the tolerance or "immunity" which is developed to both treatments. Rats tolerate progressively larger doses of MSF given intraperitoneally at 3-day intervals, and they can be "trained" to withstand a dose of 2 MLD and possibly more. Technical difficulties arise with still larger doses, for the bulk of material involved is very high (Bielschowsky and Green 1943). Another difficulty is an increasing tendency to infection after repeated injections; this may be accidental, but there is some evidence that the increased vascularity of the intestine and its supporting membranes may increase the permeability of the gut to intestinal organisms. With purer specimens of MSF this difficulty may be overcome. In comparison with this acquired tolerance to MSF, rats also develop a tolerance to hind-limb ischæmia, and large numbers have been "trained" to withstand twice the lethal ischæmic time, which is about the practical limit with

* A preparation kindly supplied by Dr. E. G. L. Bywaters.

the method used. Noble (1943) has clearly demonstrated a similar development of resistance in rats and guineapigs after a severe form of general body trauma. Here, too, there is a tendency to local infection of the thigh muscles, sometimes with a general spread. This is readily understood as the result of local trauma (though the skin is unbroken) combined with the longer survival times, though it may conceivably be caused in the same way as the infection sometimes observed after repeated doses of MSF.

The crucial point in determining whether the two syndromes are related is whether a cross "immunity," in either or both directions, can be produced. Many experiments on these lines have been made, but without results of statistical significance. The rats with increased tolerance to limb ischæmia show a tendency to withstand somewhat larger doses of MSF, but no such tendency has been seen in the reverse experiment. If for argument it be allowed that the two syndromes are related, then the reason for the relative failure of the cross "immunity" experiment may be (1) that active substances other than those contained in MSF are released from the asphyxiated limb (e.g., myohæmoglobin); or (2) that the impure muscle extracts contain sensitising or toxic substances, other than those presumably liberated in the ischæmic limb. An interfering factor is the apparent lowering of resistance to infection produced by the repeated treatments. Animals tolerant to one treatment and then given the other sometimes die from acute infection. A conclusive answer to these important questions may be obtained now that pure preparations of MSF are available.

The cumulative lethal effect of sublethal periods of limb ischæmia combined with sublethal doses of MSF is best seen if the muscle product is injected before the release of the clamps. If the dose of MSF approaches the lethal dose the effect may be very striking, for after release of the clamps the animal may die in a few minutes. With roughly half "minimal lethal doses" of each treatment, the response of the rat is roughly similar, both in nature and duration, to that seen after a "minimal lethal dose" of either treatment. The fact that the two methods reinforce each other does not establish any relationship between them. For instance, rats submitted to a sublethal period of limb ischæmia show diminished tolerance to histamine and to NaH_2PO_4 and to other agents (e.g., yeast adenylic acid and adenosine). Nevertheless, the fulminating effect described and the quantitative relationships of the combined treatments may indicate some common feature in their modes of action.

It has been frequently observed that rabbits and cats subjected to prolonged operative treatment under Nembutal anæsthesia tolerate much smaller intravenous doses of the muscle fractions. In the rabbit as little as 1/10 of the normal MLD may kill under these circumstances. A similar effect has been observed after deliberate bleeding, without anæsthesia, in rabbits. Bleeding also lowers the tolerance of rats to limb ischæmia.

All the facts set out in the table suggest that there may be features in common in the mechanism of these two experimental forms of "shock." No strikingly dissimilar features have been observed; but that may be only an indication of the necessarily limited extent of the inquiry to date. It must be recognised that many of the features of shock in animals and man are shared by other states, such as severe infections, which are not classified as "shock"; they are not, therefore, specific in any way. It is for that reason that the renal changes and the early fall in body temperature are, perhaps, of greater significance than the other findings.

MSF IN ISCHÆMIC MUSCLE

Strong support would be given to the present concept by the finding of an increase in the amount of MSF in limb muscle after a period of ischæmia. Various methods have been tried, but in none has any increase been found. Crude saline extracts (My_A) of the acetone-dried muscle from rat hind limbs, removed at intervals (final—18 hours) after release of the pressure, were made. No very significant alteration in the MLD was found at any time, but its intravenous depressor effect gradually diminished to a very low level. On the other hand, in rabbit thigh muscle removed before release of the clamp and after 4 hours ischæmia, the percentage of active material (My_C) obtained by chemical fractionation (see Bielschowsky and Green 1943) was about half that from the control opposite limb (see table II). This might be expected since the muscle is dying during the asphyxial period, and it is well established that the amount of active material rapidly diminishes after death.

TABLE II—EFFECT OF LIMB ISCHÆMIA ON ACTIVITY OF MUSCLE EXTRACT (RABBIT) (Death—acetone time, 15 min.)

—	Calculated yield per g. ADM (mg.)	No. of depressor doses/g. ADM	No. of lethal doses/g. ADM
My_C: Control limb	11·0	11	0·6
My_C: Ischæmic limb *	6·2	6	0·3

ADM = acetone-dried muscle.
Death-acetone time is the period between death of the animal and total immersion of the muscle in acetone.
* Muscle removed before removing clamp.

Incidentally, it should be mentioned that anaerobic conditions do not prevent the destruction of MSF in the muscle after removal from the body, and therefore that the process is not one of direct oxidation. Though these findings at first sight seem to contra-indicate any relationship between "ischæmic shock" and MSF, a possible explanation is given in the discussion.

Therapeutic Experiments

Following indications obtained from the published and unpublished results of other workers in the experimental treatment of traumatic shock, the following substances have been tested for possible prophylactic or curative actions, both after injection of MSF and after limb ischæmia. Given in the recommended doses, ascorbic acid (Ungar 1942), 'Nupercaine' (Ungar 1943), vitamin B_1, methylene-blue, and $NaHCO_3$ were without effect on the mortality-rates. Accurate survival times were not recorded.

Discussion

The full implication of these findings must await further elaboration and confirmation of the work. Whatever their relation, if any, to traumatic shock in man, they are in themselves of physio-pathological interest. The fact that a substance can be extracted from normal voluntary muscle which has such a profound effect on the whole organism suggests that it has some functional use—possibly of a defensive nature. Shock is not necessarily a pathological state.

The immediate practical interest is whether the syndrome produced after injection is actually shock or a non-specific shock-like state such as may be caused by any general tissue poison. We are at once brought into the vicious circle of reasoning which is inevitable in a discussion of a state which cannot yet be accurately defined. In fact, the identity of the experimental syndromes is difficult to establish unless it can be shown (1) that MSF can be isolated from the blood or tissues of the shocked animal in significantly greater amounts than in any other morbid state or in the normal animal, or (2) that an effective method of prophylaxis or treatment by the production of "immunity" to shock with MSF, or by the destruction of MSF in the body, can be devised. Concerning (1), it is quite possible that even if the postulate is true, the results might be negative or equivocal, since all the evidence suggests that MSF is rapidly destroyed in the tissues. It appears that if a certain "threshold" value is reached, even temporarily, changes occur which, according to present knowledge, are irreversible, and lead to death. Concerning (2), attempts at prophylaxis against the shock induced by limb ischæmia have met with no definite success, but it is much too early to accept these results as conclusive.

Meanwhile one can only draw tentative conclusions by the process of analogy; and in doing this the failure of the histamine hypothesis, which at the time appeared extremely sound, should be borne in mind. Nevertheless, on the basis of any of the modern definitions of shock, it would be difficult to deny that the animals treated with the muscle product are in a comparable state. They show the cardinal features of a profound depression

of all vital activities, with retention of consciousness almost till death, a low blood-volume, hæmoconcentration, a late fall in blood-pressure, a profound fall in body temperature and evidence of kidney damage. The post-mortem findings are relatively slight except for evidence of a widespread increase in capillary permeability. Less important but perhaps significant points are the increased peristalsis (with vomiting in the cat), the rapid, and usually complete, recovery from the state induced by a sublethal dose, the greater susceptibility of older animals, and the individual variability in response.

The whole syndrome is, moreover, strikingly similar to that seen when the circulation is returning to a hind limb in which the main blood-supply has been occluded for some hours. This latter method of producing shock is becoming recognised as a standard experimental procedure. It is very difficult to distinguish it, except for local hæmorrhage, from the state induced by more violent forms of trauma to the limb, and there is probably no fundamental difference between the two states. The effect of hæmorrhage may well be only that of increasing the degree of tissue asphyxia by reducing the amount of available hæmoglobin, or of decreasing the capacity of the tissues to destroy the shock factor(s). It may here be significant that bleeding the animal increased its sensitivity to both MSF and limb ischæmia.

Superficially it would seem that if MSF is responsible for some or all of the effects of muscle ischæmia, more of it should be obtained from the asphyxiated than from the normal limb; whereas in fact there is less, even when the muscle is removed before release of the circulation, and therefore presumably before any significant part could have been transferred to other parts of the body. It is, however, highly probable that the effect of the prolonged asphyxia is to increase the permeability of the muscle cells to normal intracellular constituents or metabolites. Viewed from this angle, the relevant fact would not be the quantity of MSF contained in the tissue as a whole, but its availability for resorption into the lymphatic or capillary circulation. That the amount is actually diminished corresponds with the fact that it rapidly disappears in dead muscle. It should be recognised also that in the living tissue its continuous production is possible, and that therefore in the asphyxiated limb, after release of the pressure, its formation may quickly begin again. It would continue to pass through the muscle cell membrane until the cell had recovered from the effects of the prolonged asphyxia.

In the rat a lethal dose of the crude muscle extract is roughly equivalent in terms of fresh muscle to one-fifth of the body-weight. This apparently enormous dosage is not, as might at first sight appear, outside the scale of any process likely to occur in the body. The bulk of muscle which must be submitted to trauma and/or asphyxiated in order to produce severe shock in animals or man is very large and the production of the hypothetical shock factor in the intact animal would not necessarily be static. On the other hand, in muscle dying after removal from the body the striking feature is the great lability of MSF, and a significant proportion has probably already been destroyed before the chemical extraction begins.

Duncan and Blalock (1942) showed that the survival time after hind-limb ischæmia was prolonged by the application of uniform pressure to the limb. This result may be explained by the control of local fluid loss; it can, of course, be just as well explained by the control of the rate of release of a chemical factor from the muscle into the general circulation.

It is still not clear how or where the muscle product acts. The degree of shock obviously depends on its concentration in the blood or tissues, for the survival time varies from a few minutes to a day or more, according to the dose and the site of its administration. The post-mortem findings, as in all forms of uncomplicated shock, only indicate a possible general increase in capillary permeability, and there is some evidence of an increase in the water content of the liver, kidney and brain (the only tissues examined). Vital dyes also pass more readily into the injected area and into the perfused knee-joint. All the phenomena described could conceivably be attributed to this one factor, though it must be noted that the more acute the effect the less obvious is the loss of fluid into the tissue spaces. The whole syndrome could just as well be attributed to a specific action on the nervous system, of which the capillary reactions are only an expression. In fact, the signs and symptoms are in the main similar to those produced by stimulation of the cholinergic nervous system.

All these points will be simpler to investigate now that the chemical nature of one, and possibly the only, active substance in the muscle extracts is known. Adenosine triphosphate is almost certainly responsible for the rapid lethal effect on intravenous injection, and is very probably responsible for the shock-like effects described as resulting from the injection of MSF. Experimental evidence for the latter hypothesis is not complete but the preliminary findings support it. Attempts are now being made to find whether adenosine triphosphate plays a part in the mechanism of shock produced by limb ischæmia and by other means. It is of interest that Bennet and Drury (1931) investigated the possibility of adenine compounds being released from injured tissue, and produced some tentative evidence of an increased release of such a compound from burned heart muscle. Assuming that it proves to be a factor in shock, it is unlikely to be the only one. Other physiological substances, which after release from the cell become potentially harmful, probably appear in the tissue fluids of asphyxiated tissue. Myohæmoglobin is an example, and this substance was shown to accentuate the effects produced by MSF. It remains to be seen whether adenosine triphosphate or other muscle constituents, or a combination of these, are responsible for the shock of limb ischæmia.

It would be premature to try to identify these experimental findings with those found in traumatic shock in man. There are, however, some common features which may help in the understanding of some of the more recent clinical observations. For instance, hæmoconcentration has until lately been regarded as an important indication of shock. Recent clinical investigations* fail to reveal it in the great majority of cases of severe injury, even when hæmorrhage is not considerable. It is by no means invariable, however, or at any rate may be very transitory, in our experimental animals—though here the factor of hæmorrhage does not enter. Again, in this form of experimental shock the blood-pressure may be maintained for many hours though other signs of shock are present. Similar observations have been recorded in man. Perhaps the most interesting resemblance concerns renal function. The anuria and urine changes following injection of MSF in the animal, and the clinical syndrome of traumatic anuria, appear very similar. Finally, the volume of muscle involved is undoubtedly related to the severity of traumatic shock in man as it is in this experimental condition.

The "crush syndrome" has not been considered here, though its experimental production was the goal initially aimed at. Our original hypothesis was that it was only a more chronic form of traumatic shock in which, under the peculiar conditions, one manifestation, the renal lesion, became more obvious, owing to the relatively much longer time in which severe muscle asphyxia continued. Whether this hypothesis has any value or not, there is little doubt that a disturbance of renal function is a prominent feature in shock produced by a variety of methods. Bywaters et al. (1942) have demonstrated the possibility that myohæmoglobin may be responsible for the structural and functional changes in the "crush kidney." The present finding that myohæmoglobin accentuates the lethal and nephrotoxic potency of MSF seems to have some bearing on this problem.

Summary

Some of the biological properties of a shock-producing substance extracted from fresh voluntary muscle are described.

It is rapidly destroyed in the muscle after death, which probably explains many previous failures to obtain shock-producing extracts from normal or injured muscle.

Given intravenously, it has a powerful depressant action on the blood-pressure. With a lethal dose, the size of which varies in different species, the blood-pressure fails to rise again and death rapidly ensues.

Injected by other routes it produces a prolonged shock-like state which, with an appropriate dose, proves fatal.

* Of a team working in Sheffield.

The factor responsible is referred to as the muscle shock factor (MSF). The shock-like effect is still obtained when the factor responsible for the intravenous depressor action is destroyed by acid treatment.

The effects produced by the muscle shock factor are compared with those in the shock-like state seen after occlusion of the circulation to the hind limbs. The physical signs and autopsy findings, and the pathological changes in the blood, body temperature and renal function are very similar in the two states.

The derangement of renal function by the muscle shock factor is particularly emphasised. It is accentuated by the simultaneous injection of myohæmoglobin.

Some degree of acquired tolerance to the muscle shock factor is developed. Tolerance to the effects of hind-limb ischæmia is also observed.

The conclusion is drawn that there are common features in the mechanisms of the shock-like states produced by the muscle shock factor and by hind-limb ischæmia.

Resemblances between the findings in these two forms of experimental shock and those in the traumatic shock of animals and man are also noted.

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II.—FRACTIONATION, CHEMICAL PROPERTIES AND EFFECTIVE DOSES

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THE method of preparation of the substance obtained from voluntary muscle, whose biological effects are described in the previous paper,[1] was based on that described by Dyckerhoff et al.[2] for producing "myotoxin." The method, with our modifications, is as follows.

METHOD OF PREPARATION

Dried muscle.—In the preliminary work the rabbit was used, as this was the animal used by Dyckerhoff. For production on a large scale a larger animal was required and we have used ox muscle. The animal is killed and muscle from any quickly accessible site is removed *immediately* and minced into 5–7 times its weight of cold acetone while constantly stirring. This process must be carried out with great speed, for only muscle brought into acetone within 10 minutes after death gives adequate yields of active material. The acetone is removed through muslin or a very fine sieve and the muscle is stirred again into fresh acetone (7 times original muscle weight). The acetone is removed as before and the muscle stirred again into fresh acetone (5 times the original muscle weight).

The next stage can be proceeded with at leisure. The bulk of the acetone is again removed and the muscle residue is shaken with 3 volumes of ether and then filtered with suction. The material on the Buchner funnel is washed with 2 volumes of ether. The muscle residue is spread out on filter paper in a thin layer and the ether allowed to evaporate off at room temperature. The final drying is made in a vacuum desiccator over $CaCl_2$: the dried material is then finely powdered, care being taken that no heat is produced during the process.

Crude saline extract (*Mya*).—The dried muscle powder is stored in the refrigerator and used as required. In this form it appears to remain stable indefinitely. It is worked up into suitable batches according to requirements; the further procedure given is for an amount of 250 g. This is mixed with 1250 ml. of saline and extracted for 7 minutes at room temperature on a shaker. The mixture is at once pressed through cloth of fine texture; the filtrate is brought quickly to boiling and after 7 minutes is quickly cooled to room temperature. The precipitate is removed by filtration (Whatman paper No. 54) and the filtrate (Mya), if required for biological tests, is Seitz-filtered.

Alcohol precipitate I (*Myb*).—The clear filtrate (Mya) is ice-cooled and 3 volumes of ice-cold CH_3OH are added whilst stirring; it then remains in the cold for 2 hours. The precipitate is centrifuged down, the clear supernatants decanted and discarded. The precipitate is resuspended in the centrifuge tubes with CH_3OH (approximately twice the volume of precipitate). The washing is repeated and the precipitate given 2 washings with ether.

Instead of using the centrifuge to obtain the CH_3OH precipitate, it may be collected on a Buchner funnel (Whatman No. 50 smooth) and then washed twice with CH_3OH and twice with ether, taking care that the precipitate is always covered by fluid until the operation is completed. The resulting white cake, from either method, is quickly broken up and the ether evaporated off in a vacuum desiccator.

Alcohol precipitate II (*Myc*).—Batches of 5 g. of the precipitate (Myb) are placed in a mortar and dissolved in 250 ml. boiling saline, which is added in small portions, mixing well each time. The solution is transferred into a fairly large beaker (there is a danger of frothing) and boiled for 3 minutes. It is cooled quickly to room temperature and filtered (Whatman No. 5). To the clear filtrate 3 volumes of CH_3OH are added. The further treatment is similar to that described for Myb. The yield of Myc from rabbit or beef muscle is around 1% of the dry muscle. A further quantity, bringing the total yield up to 1·6–2·0% can be obtained by re-extracting the dried muscle residue with saline and pooling the two extracts.

For technical purposes it is convenient to retain in this paper the symbols used above. The term "muscle shock factor" (MSF) used in the preceding paper [1] is a convenient expression of part of the biological activity of preparations Mya, Myb, Myc and others to be described.

CHEMICAL PROPERTIES

Myc is a white amorphous non-hygroscopic powder. It is soluble in water, giving a clear solution, up to 10% at room temperature. In dilute HCl it dissolves more quickly, while in dilute NaOH it forms a very opalescent solution; it has no melting-point; discoloration starts at 195° C. and goes on to complete carbonisation. It can be reprecipitated from watery solution by the addition of three volumes of methyl alcohol or 4 volumes of acetone. It contains non-protein nitrogen. It gives a weakly positive reaction to all tests for protein (biuret, Esbach, Sakaguchi, Millon, Pauly, ninhydrin). The orcinol and Molisch tests are strongly positive; Fehling's test is negative; the Dische (desoxy-sugar) test is negative. It contains traces of glycogen. It is rich in phosphorus, containing about 6% in the organic form, and contains magnesium but no potassium. The inorganic residue after incineration is on the average 30%.

In the dry state it retains its biological potency for an indefinite period. In neutral solution, in the cold, the depressor activity showed no alteration in 4 weeks; its potency in MSF was probably not altered but results were erratic.

RELATION OF YIELD TO TIME OF EXTRACTION

It was not always possible to get the whole of the muscle into acetone within 10 minutes of killing the animal. With the rat it was, and with the rabbit it usually was, but with the ox, killed in the abattoir, the time was usually longer. In table I a representative selection from the available data is made. It will be seen that the number of lethal doses per gramme dried muscle fell rapidly in both rabbit and ox muscle as the interval after death increased. Refrigeration did not prevent this, though it probably diminished the rate of loss. The LD_{50} of Myc from rabbit muscle appeared to remain fairly constant whether the yield was large or small; in contrast that of Myc from beef appeared to increase as the yield fell. This fall in the lethal dose was not directly proportional to the yield and is possibly an

1. Green, H. N. *Lancet*, 1943, ii, 147.
2. Dyckerhoff, H., Schorcher, F. and Torres, I. *Biochem. Zschr.* 1939, **300**, 198.

TABLE I—RELATION OF TIME BETWEEN DEATH OF ANIMAL AND IMMERSION OF WHOLE OF MUSCLE IN ACETONE, TO YIELD AND INTRAPERITONEAL LETHAL DOSE OF MUSCLE PREPARATIONS

Preparation	Time between death-acetone (min.)	Yield /g. ADM* mg.	Calculated yield /g. ADM* mg.	LD_{50} /10 g. mouse mg.	No. lethal doses /g. ADM
My_a rabbit (av. figure)	10	3·5 ml.	5·0 ml.	1·8 ml.	2·8
My_b rabbit (av. figure)	10	12·5	20·0	40	0·5
My_c rabbit (av. figure)	10	10·0	16·0	17·5	0·9
My_c rabbit control	20	6·2	8·4	30	0·3
My_c (rabbit)	16 hrs. at 5° C.	2·1	2·6	30	0·1
My_c (ox)	15	10·2	17·4	20	0·9
My_a (ox)	60	7·7	12·2	80	0·15
My_c (ox)	Overnight	2·1	3·6	60	0·06

* ADM = Acetone-dried muscle.

expression of the greater percentage of impurities in the beef preparations. These were made on a commercial scale and did in fact always contain varying amounts of insoluble matter which was not present in the rabbit material.

It should also be noted (see table III) that the crude preparation, My_a, from rat muscle gave the highest yield of lethal and depressor doses per gramme dried muscle of any preparation tested. This is probably due to the rapidity with which the whole of the rat muscle could be immersed in acetone.

LETHAL POTENCY OF VARIOUS FRACTIONS

In table II average figures are given for the LD_{50} of My_a and My_c injected by the intravenous or intraperitoneal routes. The figures are only approximate, for both individual and strain variability are very great, while age, general condition and unknown factors affect the responses. They give however a working guide to the activity of the extracts when the prescribed methods of preparation are accurately followed.

It will be seen that the activity of the crude saline preparation, My_a, is roughly three times that of My_c. It was found that roughly two-thirds of the lethal and depressor potencies of My_a remains in the filtrate after the first CH_3OH precipitation. Assuming that this activity is all due to unprecipitated My_c, the amount of My_c in the dried muscle is some three times that of the calculated yield by this method.

The first CH_3OH precipitate, My_b, was considerably less lethal by the intraperitoneal route than the second precipitate, My_c (tables I and III). This increase in potency from My_b to My_c is probably due to the removal of a substance which slows down the absorption of the active principle. This explanation is supported by the finding that they had an equivalent depressor activity on intravenous injection (tables I and III). There was a general tendency for the yield of lethal doses to increase progressively at the various stages of purification from My_b onwards.

The intravenous lethal dose is very much less than the intraperitoneal lethal dose, ranging roughly from 1/5 to 1/15 in different species (cat excepted). It is probable, however, that this difference is not merely an expression of the relative blood concentrations attained, for the mechanism by which death is produced is probably not the same by the two routes of injection. Intravenously, death is due to a profound and sustained fall in blood-pressure, whereas a fall in BP is not the primary cause of death after injection by other routes.

As might be expected, large doses are well tolerated by mouth, and rats show little signs of being affected when an oral dose much larger than the lethal intraperitoneal dose is given.

SPECIES SENSITIVITY

Different species show wide differences in their tolerance to the extracts (table II).

The lethal doses for the mouse and rat are closely related and so are those for the rabbit and guineapig; but the latter animals are much less resistant than the former. For instance, the intravenous lethal dose in the mouse is 10 times that in the guineapig, whereas the corresponding ratio for the peritoneal route is only 4. A similar type of relationship holds for the rabbit. This difference is again probably an expression of the difference in the mechanism of death after injection by the intravenous or other routes.

In both the rabbit and guineapig individual variability is pronounced.

Though the intravenous LD_{50} of My_c in the rabbit is given as 5 mg./100 g. body-weight one is occasionally surprised by seeing an apparently normal animal die in a minute or two, even after such a small dose as 0·25 mg./100 g. Some, but not all, of these "normal" animals proved to have a chronic lung infection at autopsy. On the other hand young rabbits have been observed to tolerate doses of 10 mg/100 g. without showing more than a transitory reaction. This extreme variability renders the rabbit quite unsuitable for biological assays.

The cat is the most tolerant animal of those tested. Owing to the large amount of material required, only a few tests of lethal potency were made on cats; so the figures given are very approximate. The high intravenous dose, as compared with the rabbit, probably reflects the much greater stability of the cat's cardiovascular system. The enormous intraperitoneal dose, as compared with the rabbit, may conceivably reflect the much greater tolerance of the cat to all forms of tissue trauma.

TABLE II.—LETHAL DOSES (LD_{50}) OF MUSCLE PREPARATIONS IN VARIOUS SPECIES (PER 100 G. BODY-WEIGHT)

	My_a				My_c			
	Intravenous equiv.		Intraperitoneal equiv.		Intravenous equiv.*		Intraperitoneal equiv.*	
	Dose ml.	ADM g.	Dose ml.	ADM g.	Dose mg.	ADM g.	Dose mg.	ADM g.
Cat ..	..	..	..	..	20†	1·25	600	38·0
Rat ..	3	0·6	18	3·6	20	1·25	175	11·1
Mouse ..	4	0·8	18	3·6	30	1·9	175	11·1
Rabbit ..	0·5	0·1	..	..	5	0·3	60	3·8
Guineapig	0·4	0·08	6	1·2	4	0·25	40	2·5

ADM = Acetone-dried muscle.
* Based on calculated yield of 1·6%. † During anæsthesia.

COMPARISON OF DEPRESSOR AND LETHAL POTENCIES

Table III shows a fairly close correlation, considering that two biological tests are involved, between the activity of the preparations in lowering the BP on intravenous injection and their lethal potency on intraperitoneal injection. It will be observed however that the ratio of depressor to lethal dose is distinctly higher in the more active than in the less active beef preparations. This observation is probably not of great significance, for it may be merely an indication of the relative increase in impurities with decreasing yields of My_c from ox muscle. Some part of these impurities, though having no depressor action, may have a non-specific toxic action which results in a relative fall in the lethal as compared with the depressor dose.

This lack of correlation, in some of the preparations tested, initially caused doubt as to the identity of the depressor and lethal factors, and this was increased by other observations,[1] particularly the results of acid hydrolysis. While acid hydrolysis (see table III) completely destroyed the depressor activity, it only reduced the lethal potency by about one-third. This suggested a lack of identity between the depressor and lethal factors. But results of further fractionation have in part resolved these difficulties.

FURTHER FRACTIONATION OF MY_C

The more elaborate chemical details will be published elsewhere by one of us (M. B.). So only the outlines need now be given.

Dialysis.—The dialysates of the various fractions already described were not consistent in their biological effects and will not therefore be considered further here.

Removal of proteins (My_S).—The bulk of the proteins are removed by treating My_C with saturated salicylic acid (pH 4·5) and ice-cooling. Reprecipitation with CH_3OH yields 75% of a preparation which contains only a trace of protein; sulphosalicylic acid gives only slight turbidity and all the other protein reactions are negative. This product, My_S, is easily soluble in water and the reaction of the solution is neutral. Its ash content is, on the average, 25%. It retains the full biological activity of My_C. Its depressor activity is increased proportionately (25%) but the lethal potency is increased disproportionately (around 100%). This apparent increase from My_C to My_S is probably due to an increase in the rate of absorption after injection.

Precipitation with acridine.—From the early stages the biological tests had indicated that the depressor substance was probably an adenine compound. The results of chemical analysis also favoured this view; for adenine was isolated after acid hydrolysis, the pentose reaction was positive and the substance was rich in acid-soluble phosphorus. The confusion as to the identity of the depressor and MSF factors could only be resolved by removing the postulated adenine compound from My_S. This was attempted by precipitation with acridine. The acridine precipitate formed about 40% of My_S and contained a high percentage of adenosine triphosphate; it possessed most of the depressor activity of My_S. The acridine-free filtrate had still a slight depressor action, whilst the lethal potency appeared to be fairly equally distributed between the two fractions. Precipitation of the filtrate with CH_3OH yielded a substance (36% of My_S) which had only a feeble depressor activity but about half the lethal activity of My_S.

Precipitation with barium chloride.—The precipitate (65% of My_S), freed from Ba, and allowing for possible losses in chemical manipulation, contained all the depressor and lethal activities of My_S (table III). The Ba-free filtrate gave, on addition of CH_3OH, a small precipitate (about 4% of My_S) which had no depressor or lethal activity.

The barium precipitate was proved to contain a high percentage of adenosine triphosphate by analysis of its adenine content in the form of the picrate and by determinations of the 7 "mins" P. Reprecipitation with mercuric nitrate and barium acetate yielded a substance which analysis showed to be pure barium adenosine triphosphate. Preliminary tests with the sodium salt of this compound indicated that it possessed the full depressor and lethal potencies of the My_C from which it was prepared (table III). Moreover the yields obtained (30–40% of My_C) appear to be directly related to the biological potency of the samples of My_C from which they were prepared.

TABLE III—DEPRESSOR ACTIVITY OF MUSCLE PREPARATIONS ON BLOOD-PRESSURE OF CAT COMPARED WITH INTRAPERITONEAL LETHAL POTENCY IN MOUSE

Preparation	Dose producing fall of 30 mm. Hg/k. body-wt. ml.	No. depressor doses g/ADM	No. lethal doses g/ADM	Depressor/lethal ratio
My_A (rat)	0·02	250	5	50
My_A (rabbit)	0·04	125	3·3	38
OX				
My_A	0·06	82	2·5	33
	mg.			
My_B	0·6	33	0·5	66
My_C	0·5	35	0·9	39
My_C	1·0	9	0·5	18
My_C	2·0	8	0·4	20
My_C	2·8	1·3	0·15	9
My_C	1·2	15	0·4	38
My_S	0·8	17	0·6	29
My_S	1·0	15	0·4	38
Na salt of Ba precipitate from My_C	0·4	11	0·3	37
My_C	0·5	20	0·5	40
Na adenosine triphosphate from My_S	0·3	23	0·7	33
Adenosine	0·6	..	..	..

Effect of Acid and Alkali Treatment on My_C
(N HCl and N NaOH, 30 min. at 100° C.)

My_S	0·6	13	0·4	33
My_S (alkali-treated) ..	0·6	13	0·3	43
My_C (acid-treated) ..	5·0 +	0	0·25	0
My_C " " ..				
CH_3OH precipitate ..	5·0 +	0	0·3	0

CONCLUSIONS

The results of chemical fractionation of saline extracts of the acetone-dried muscle strongly suggest that adenosine triphosphate is the substance mainly responsible for the described biological effects of the muscle extracts. It therefore probably corresponds to the muscle shock factor (MSF) described previously[1]; and though this remains to be proved, all the preliminary tests support this view. It certainly is the active depressor substance and therefore responsible for the rapid lethal effect on intravenous injection in the rabbit. Inosine triphosphate has no significant depressor action. Adenosine triphosphate is identical therefore with myotoxin as described by Dyckerhoff.[3]

The fact, however, that acid hydrolysis for 30 minutes destroyed the depressor activity but only reduced the MSF activity, has still to be accounted for. This point has already been considered[1] in its biological aspects, but some chemical considerations are relevant. The toxic nature of the ash obtained by incineration provided a possible clue.

Tests with the ash at an early stage of the investigation suggested that its lethal potency was low and in any case of little importance since inorganic pyrophosphate, in itself poisonous, must be present in the ash of a substance so rich in phosphorus. Moreover, the pyrophosphate obviously did not exist in this form, at any rate in significant amounts, in living muscle. Neither did the fact that the lethal potency of the muscle so rapidly diminishes after death suggest that it was due to an inorganic salt. However, further consideration of this problem suggested that the insolubility of the ash might have been responsible for the indecisive assays of the lethal dose. Further tests with ash, made more soluble by acid treatment, showed that its lethal potency could be roughly related to that of the original substance. This relationship appeared to hold—a finding still unexplained and which needs further confirmation—even when the lethal activity of the parent substance was low.

These findings directed attention to the possible rôle of pyrophosphates in the shock-like state induced by the muscle extracts. With the isolation of adenosine triphosphate strong support was given to the hypothesis that the effects of MSF are in some degree—probably a large one—linked with the pyrophosphate radicle. If this is so, accumulated knowledge of the important rôle of pyrophosphoric acid in many biochemical reactions should help in elucidating the pathological reactions produced by the muscle shock factor.

SUMMARY

The mode of preparation of a shock-producing substance present in striated muscle is described.

Evidence is given of its rapid destruction in the muscle after death of the animal.

The lethal and blood-pressure-lowering activities of the chemical fractions are stated, compared and discussed. The lethal dose in different species varies widely: it is much higher in the cat, rat and mouse than in the guinea-pig and rabbit.

Fractionation of the muscle preparations resulted in the isolation of adenosine triphosphate in large amounts.

Reasons are given for the conclusion that adenosine triphosphate is the substance responsible for the rapid death following intravenous injection of the muscle extracts. Probably it is also responsible for many or all of the features of the shock-like state which follows injection by other routes.

The expenses of this work were defrayed by the Medical Research Council. One of us (M. B.) receives a part-time grant from this source. We are much indebted to Mr. W. A. Broom and Mr. R. Falconer of Boots Pure Drug Co., Ltd., for their helpful collaboration in the large-scale production of the muscle products.

SERIAL SPINAL ANALGESIA

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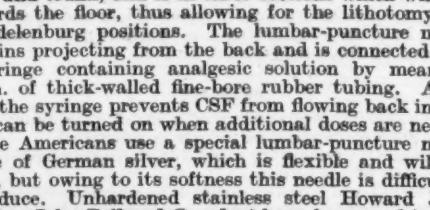
SPINAL analgesia has undergone many improvements since its discovery by Corning (1885), and its introduction into clinical medicine by Bier (1899). Modern interest was revived by the discovery of ephedrine by Chen and Schmidt (1926) and its use to combat the fall in blood-pressure during spinal analgesia by Ocherblad and Dillon (1927). Other drugs used in anæsthesia are given in continuous or serial dosage, according to the patient's needs, and it has always been held against subarachnoid block that the drug must be injected by the one-shot method. Thus Lemmon's first paper (1940) on continuous spinal anæsthesia was an important step forward. Later, Edwards and Hingson (1942) modified the technique for use in obstetrics as continuous caudal analgesia.

Lemmon used procaine ('Novocain') because of its lack of toxicity, the rapid onset of analgesia and the relatively short duration of action. Later Nicholson and his colleagues (1941) used amethocaine hydrochloride ('Pontocain'). 'Nupercaine' has also been used. Lemmon employed several strengths of procaine solution, all of them being greater than 3%. Fraser (1943) has recently published a series of cases using 1% procaine in saline, with which he is well pleased.

In this small series a start was made with procaine crystals dissolved in cerebrospinal fluid, but there was difficulty in getting the analgesia high enough for upper abdominal work; moreover, the preparation of the solution took too much time. Procaine, 5%, in normal saline was tried but was not as controllable as the final choice which has given considerable satisfaction. This is 5% procaine in 5% glucose, with a specific gravity of 1026, making it hyperbaric.

Equipment.—Serial spinal analgesia is made possible by placing the patient on a specially built mattress, 5 in. thick, which lies on the operating table, and has a cut-out part, 12 in. long, beneath the lumbar spine (see figure). The part beneath the buttocks, thighs and



legs is detachable from the upper part supporting the head and trunk, and is in three sections which will flex towards the floor, thus allowing for the lithotomy and Trendelenburg positions. The lumbar-puncture needle remains projecting from the back and is connected with a syringe containing analgesic solution by means of 30 in. of thick-walled fine-bore rubber tubing. A tap near the syringe prevents CSF from flowing back into it, and can be turned on when additional doses are needed.

The Americans use a special lumbar-puncture needle made of German silver, which is flexible and will not snap, but owing to its softness this needle is difficult to introduce. Unhardened stainless steel Howard Jones needles (John Bell and Croyden) have been used instead and have caused no anxiety. On several occasions the needle has been found bent on withdrawal, but there have been no breakages.

TECHNIQUE

The premedicated patient with plugged ears and shaded eyes is given an injection to maintain the blood-pressure such as pholetone 10 mg., and is then placed in the left lateral position in such a way that the selected interspace corresponds with the gap in the mattress. A weal is raised and a Rowbotham's introducer is driven into the ligamentum nuchæ. The lumbar-puncture needle is then placed in the subarachnoid space through the introducer, which has three advantages: it prevents contamination of the needle by the skin edges; it provides splintage for the needle; and it fixes the needle by means of the screw cap at its distal end. It has the disadvantage that it masks the characteristic click felt when the needle pierces the dura.

The height of analgesia is controlled by the level at which the injection is given, by barbotage, by the rate of injection, by the tilt of the table and by the amount of drug injected. For upper abdominal work the second interspace is used, for mid-abdominal operations the third interspace, while for lower abdominal and perineal procedures the fourth interspace is selected. A rough estimate of dosage is to give 1 mg. of procaine for each lb. of body-weight, taking into consideration the build and general condition of the patient and the height of analgesia required.

When CSF runs freely, the needle is locked in position and the initial dose of procaine-glucose solution is injected direct from a syringe. This usually varies from 100 to 150 mg., or from 2 to 3 c.cm. The stilette is put back and the patient is turned into the supine position so that the protruding end of the needle lies in the gap in the mattress. This manœuvre requires care as clumsiness may result in the displacement of the point of the needle from the subarachnoid space. The patient should be told not to help himself round, but to lie as a dead weight to be lifted into the new position.

With the patient flat on his back the anæsthetist, who has kept his hands sterile, removes the stilette from the needle to see that CSF is dripping. Slight manipulation or rotation of the needle may be required to ensure a steady flow. The sterilised rubber tubing which has been filled with solution and emptied of air bubbles, and has one end attached to the solution containing syringe and tap, now has its other end plugged into the lumbar-puncture needle by means of an adapter. A bayonet-fitting is ideal for this. Finally, the syringe is fixed to the head of the mattress with adhesive strapping. If, on opening the tap, CSF can be aspirated into the syringe the technique is correct.

For lower abdominal operations the table remains level, while for upper abdominal procedures a 5° Trendelenburg tilt is required to send the solution to the proper level, and the head should be well flexed on a sandbag to prevent the solution from going higher than the fourth or fifth dorsal segment. Height of analgesia is tested frequently during the first ten minutes, and the table levelled off when it reaches to the nipple line. If in ten minutes the analgesia has not ascended high enough, a further dose of 50 mg. of procaine (1 c.cm.) is injected. Fixation of the drug is complete within ten minutes, and thereafter any position of the patient may be assumed without fear of further spread of analgesia.

For operations likely to be short the syringe contains 5 c.cm. of solution, and for those expected to last over 1½ hours, 10 c.cm. Additional doses of solution can be injected as required, and Lemmon suggests that each half-hour 30–50 mg. should be injected. The signs of procaine insufficiency are discomfort shown by the patient, together with dilatation of the previously contracted gut, and rigidity of the abdominal wall. It should of course be the aim to forestall the appearance of these signs. In upper abdominal cases, the table should again be placed in a slight Trendelenburg tilt before supplementary injections are made; 1½–2 minutes are required for the effects of the fresh drug to act on roots previously procainised.

It has not been my experience that withdrawal of CSF after injection has shortened the period of analgesia. Lemmon on the other hand, with his vastly greater experience, claims that withdrawal of CSF rapidly causes the effect to pass off. Should the circulation collapse very shortly after either the initial or subsequent doses have been given, aspiration of fluid would be a rational procedure.

In most upper abdominal operations I prefer to have the patient asleep, and light cyclopropane anæsthesia, in which the atmosphere breathed has a high oxygen content, is the safest and most convenient way of assuring this. Alternatively, repeated small doses of 'Pentothal' can be injected, while the patient is given oxygen inhalations if and when they are required.

RESULTS

So far the method has been used in 105 cases, and in view of the newness of the technique the results have

been gratifying. Below is a list of cases with the average doses required.

Operation	Cases	Average dose (mg.)
Acute appendicectomy	1	150
Partial gastrectomy	9	430
Interval appendicectomy	10	130
Reconstruction gastrectomy	1	700
Repair of inguinal hernia	25	160
Repair of bilateral inguinal hernia	1	200
Suprapubic removal of carcinoma of bladder	3	140
Removal of pancreatic cyst	1	300
Pyloroplasty	1	450
Operations on the biliary tract	3	325
Ligature of external iliac aneurysm	1	250
Colostomy	2	200
Bilateral varices	1	150
Repair of femoral hernia	2	135
Alexander Adams operation	10	150
Gilliam's suspension	5	120
Fothergill's operation	2	115
Exploratory laparotomy (upper abdomen)	5	220
Anterior and posterior colporrhaphy	1	100
Cure of varicocele	1	140
Removal of ovarian cyst	3	120
Abdominal hysterectomy	4	160
Vaginal hysterectomy	7	140
Interposition of uterus behind bladder	6	120

In several cases the surgeon needed the patient in a steep Trendelenburg position and in these additional doses of procaine were run in, a few milligrammes at a time to prevent the analgesia spreading too high.

A young woman of 19 who was to have a chronic appendix removed failed to develop any analgesia after the injection of 150 mg. of procaine. As she was ill at ease and unhappy at not being put to sleep, cyclopropane was given and larger doses of procaine were not tried. One patient in whom the technique of spinal puncture seemed perfect required 700 mg. of procaine during 1½ hours to maintain adequate relaxation of his upper abdominal wound. This was the largest dose given in the series. Another patient, a robust soldier got indifferent relaxation in the muscles of his inguinal region after the injection of 250 mg. In this case analgesia was adequate and the hernia was repaired without the need of further procaine. A hypertensive female of large build was having an ovarian cyst removed. The lumbar puncture resulted in a free flow of CSF and 100 mg. of procaine was injected; towards the end of this injection the plunger of the syringe was slightly withdrawn and almost pure blood entered the syringe. Analgesia and relaxation were both perfect and lasted throughout the operation, but the blood clotted in the lumen of the needle, blocking it. This patient complained of neither headache nor vomiting postoperatively.

Blood-pressure readings did not differ from similar readings using the one-shot technique in operations on the lower abdomen, but in upper abdominal surgery the method makes it easier to maintain the blood-pressure as the total dosage of procaine is spread over the operating time instead of being given all at the beginning. The postoperative headache incidence has not been influenced for either good or bad by the method.

Lemmon and Paschal (1942) report that they have given over 1000 consecutive serial spinal anæsthetics and have only had to supplement one case with general anæsthesia. This is an excellent record which could be achieved only by the use of the technique described. I fully agree with them that with increasing experience the total dosage of procaine used tends to go down.

No deaths have occurred in this series that could be in any way ascribed to the method of anæsthesia.

INDICATIONS

The method is more fussy than single injection subarachnoid block, but the difficulties are technical and are overcome with practice. On the other hand there are advantages: the small initial dose makes for safety; and the occasional patient who requires a larger dose than the average is spared the unpleasant experience associated with failure of a single dose to act.

When it is decided that a case is to be operated on under spinal analgesia the serial technique is indicated when the duration of operation is expected to be long or is uncertain, since the method makes it impossible for the effects of the drug to wear off before the surgeon has completed his work. It is indicated when the scope of the operation is uncertain: for example, an operation may be thought to be confined to the pelvic organs and a dose of analgesic drug sufficient to give analgesia to the tenth dorsal segment is injected. Discomfort results if parts of the stomach or omentum require to be subjected to traction, as in freeing of adhesions. Extra procaine injected before this part of the proceeding will ensure the comfort of both patient and surgeon. Lastly, in patients who are in poor condition, when a spinal analgesic is to be given, it is preferable to space the dose over the total time of operation, rather than to give it all at once. Moreover a minimum amount can be injected and later added to if necessary.

CONCLUSION

Serial spinal analgesia is worthy of further trial in this country. It gives flexibility and control more nearly approaching that experienced during the administration of general anæsthetic drugs. Nosworthy's (1941) suggestion that, when a new drug and a new technique are to be used together, one should first become familiar with the new drug used by old and well-tried methods, is especially applicable to this method of spinal block.

SUMMARY

The advantage of continuous spinal analgesia, as introduced by Lemmon, is that the drug can be given according to the patient's and the surgeon's needs.

In a series of 105 cases reported here 5% procaine in 5% glucose was injected into the spinal theca in serial doses.

The technique described requires a specially built mattress for the operating table with part cut out beneath the lumbar spine. The lumbar-puncture needle remains in the back throughout the operation and is connected to the syringe containing the analgesic drug by rubber tubing.

A list of average doses for various operations is given. Results have been good.

I would like to express my thanks to Mr. Rodney Maingot and to Dr. Rolf Ström-Olsen for encouragement with this work.

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DOGS AS A SOURCE OF LEPTOSPIRAL INFECTION IN MAN

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With the technical assistance of E. VINCENT

On the continent leptospirosis in dogs is of two types, one due to *L. icterohæmorrhagiæ*, the other (Stuttgart disease) to *L. canicola* (Schüffner 1934). In the United States of America the latter type is by far the commoner (Meyer et al. 1939). In Great Britain, however, the only canine infection so far recognised is by *L. icterohæmorrhagiæ* (Okell et al. 1925). The observation by Stuart (1938) of a serological reaction between *L. canicola* and the serum of a human adult without either leptospirosis or special connexion with dogs does not go far to prove the existence of that microbe in this country.

On the other hand, various pieces of evidence have come our way which strongly indicate that English dogs suffer infection with a leptospira serologically different from *L. icterohæmorrhagiæ*, *L. canicola* and other types known in Western Europe.

In the course of experiments on leptospirosis of mice we examined by cross-agglutination tests a number of leptospiral cultures including—as we were advised by Professor Schüffner—all the pathogenic types hitherto known to occur in Western Europe. (*L. sejroe* was not then available.) While a general confirmation of the accepted constitution of the group resulted from the tests, certain matters not covered by the continental classification came to our notice (see table).

Two strains—"McIntyre," given me by Major H. C. Brown, and *L. icterohæmorrhagiæ* (spaniel) No. 5260 of the national collection of type cultures—proved to be serologically distinct from the 4 known types that were tested, but identical with each other. On inquiring about the origin of "McIntyre," we learned from Major Brown that its host was a veterinary surgeon who had been working on leptospirosis in dogs, and particularly with a strain isolated from a dog. He became infected and the culture was isolated from him. These two strains, therefore, both presumably originated from dogs, and since they proved antigenically distinct from the continental *L. canicola* (of which two strains of diverse origin were used) we could only conclude that they represent a hitherto unrecognised British canine type.

Sera (rabbit)		Formolised serum-water suspensions					
		A	B	C	D	E	F
A	*L. icterohæmorrhagiæ*, Jackson.	2500	100	100	0	0	..
B	*L. canicola*, Roesch	320	1280	320	0	0	..
C	*L. grippotyphosa*	200	80	1280	20	0	..
D	*L. bataviæ* ..	80	200	50	5120	0	..
E	*L.* 5260 (spaniel)	0	0	20	0	2500	..
F	*L.* "*McIntyre*" ..	0	..	..	..	2000	2000

2500, &c. = end-point of agglutination at a dilution of 1 in 2500, &c.
0 = no agglutination at 1/20 and under.

NB.—Minor agglutination may be due to factors other than specific antibodies.

In an attempt to collect further information about human infection with this microbe we have tested with *L. icterohæmorrhagiæ* 5260 some 430 human sera sent for the agglutination test for Weil's disease, and in 1 case only have we seen a positive result.

Apart from his being a farmer, and therefore certainly associated with dogs, the history of the patient's infection was not obtainable. On the 6th day of his illness he was jaundiced, but his serum failed to give significant agglutination with any of the 6 types of leptospira tested—viz., *L. icterohæmorrhagiæ*, *L. canicola*, *L. sejroe*, *L. bataviæ*, *L. grippotyphosa*, and L. 5260 (British canine). A further sample taken on the 15th day, when the patient was reported to have fever, muscle pains, vomiting, leucocytosis and jaundice, gave agglutination with L. 5260 up to 1 in 80 and with *L. icterohæmorrhagiæ* at 1 in 20, the other strains not being agglutinated at all. A third blood sample 6 days later gave a positive reaction with L. 5260 and *L.* "*McIntyre*" up to 1 in 1280, and to *L. icterohæmorrhagiæ* at 1 in 80. The patient made a good recovery.

This, then, must be judged to have been an infection with the 5260 and McIntyre type of leptospira, so that we have now two recorded cases of this kind, the patient McIntyre himself being the first.

It should be noted that practically all the human sera sent for diagnosis were from already jaundiced patients, a principle of selection which must greatly reduce the probability of detecting non-icterogenic forms of leptospirosis. For it is well known that jaundice is rare in all leptospiral infections except Weil's disease, and even in that its frequency is less than 60% (Walch-Sorgdrager 1939).

To sum up, we believe that the facts presented go far to prove the existence of a hitherto unrecognised type of British canine leptospira, transmissible to man, and differing from the continental *L. canicola*. Owing to the difficulties of war conditions we have not excluded the possibility of its identity with other types of leptospira found in the East, but there does not seem to be any reason to expect this. It is hoped that other workers may obtain further evidence.

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SUDDEN SENESCENCE

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ON March 7, 1941, a man aged 40 was admitted to our emergency hospital suffering from severe depression and headaches.

He was happily married to his second wife, with two children by his first. He was an engine driver, who had suffered in the past from no serious disease. On May 8, 1940, when in perfect health, he slipped and fell from a stationary engine, probably falling on one hand, which he remembers drawing hurriedly aside to avoid a heap of hot cinders. He tried to rise but was unable to do so because "everything went hazy and he rolled over." He continued to "feel hazy," recovering full consciousness for short intervals only for some hours. On a stretcher on the way to the hospital he had a shivering attack. When his wife came to see him he wept copiously. For five days he complained of intense headache and for three days his movements were very slow and he could neither wash nor feed himself, and was too weak to sit up. He then began to improve, and at the end of six days was able to get up. As there was no history or sign of head injury and an X ray of his skull was normal, he was discharged on the eighth day. For three months he was unsteady in his gait. From the time of the accident he felt himself to be a feeble old man. He lost all sexual desire and power and was irritable and given to self-pity. His appetite became extremely bad and he suffered from insomnia, vague frontal headache, photophobia, and giddiness at the cinema and after the smallest amount of beer.

His scalp hair began to come out on the day of the accident, at first in a round patch diagnosed as alopecia areata. The patch spread and by September or October, 1940, he was completely bald. He remained so until December, 1940, when a few white downy hairs appeared. Shortly before we saw him, a few dark hairs began to grow. In December, 1940, the hair of his limbs and trunk came out in patches and after a short time entirely disappeared. He had habitually shaved once and sometimes twice a day, but from the time of the accident he found it necessary only once a week. The axillary and pubic hair remained normal until after he came under our observation, when it gradually became sparse and grey.

On examination, he proved to be a man of very fine physique and powerful musculature. The skin of his body was smooth and fine but the face was wrinkled and old beyond his years. The blood-pressure was 148/90 mm. Hg. During his time in hospital the resting pulse-rate varied between 60 and 88 per min. and the temperature between 96·2° and 98·6° F. There was a soft systolic apical murmur. His abdominal reflexes were not elicited. His genitalia were normal.

His blood-count was: hæmoglobin 86%; erythrocytes 4 million; CI 1·07; leucocytes 9000, in normal proportions. The urine was normal in all respects. The resting blood-sugar was 78 mg. per 100 c.cm., and, in successive half hours after 50 grammes of glucose, 122, 139, 114, 90. Cutler, Power and Wilder's test for adrenal cortical deficiency was within normal limits (urinary chloride 50 mg. per 100 c.cm.). The Wassermann reaction was negative. Cerebrospinal fluid was normal. X ray of the skull showed no abnormality. There was complete achlorhydria. It was unfortunately impossible to estimate the 17-ketosteroid excretion or the basal metabolic rate.

Psychological note (A. S. P.).—From the psychological point of view the most striking symptom was that when his hair came out and he began to feel a feeble old man he became depressed and full of self-pity. He felt unnatural in his attitude towards his wife and also his son. He could not feel natural affection and he realised that this was a sign of illness. He went off his food and his weight went down from 12 st. 13 lb. to 11 st. 9 lb. He also slept badly. There was, however, no suicidal tendency. The battle of Britain began three months after the onset of his illness and he was excessively apprehensive, not relatively indifferent as one might have expected. Whereas he had previously been a non-smoker, he now smoked 40–50 cigarettes a day. He gave the impression of being a man with character and ability above the average. He spoke in a quiet dispassionate way about his illness and his future prospects. He was anxious to get back to work but doubted whether he was capable of driving an engine. He appeared to be mildly depressed, but his mood was quite consistent with his pitiable physical state. Con-

SERIES OF PORTRAITS TO SHOW CHANGES FOLLOWING ACCIDENT IN MAY, 1940

March 1940 March 1941 March 1942 February 1943

siderations of compensation did not seem primarily to come into the case. He had served as a fireman for a long time and had recently achieved his ambition of becoming an engine driver. He had no very obvious domestic worries. His intellectual functions were unimpaired.

Progress.—During two months in hospital he improved considerably. He regained 6 lb. of his lost weight, and became more cheerful. There was a slight increase in scalp hair, but no change in other areas. In July, 1941, he reported that he was "getting along fairly well," but was still impotent. In September, 1942, he reported that the hair of his head was growing fairly well, but his eyelashes, eyebrows and body-hair less well. He still felt tired after exertion and was subject to occasional attacks of giddiness after eyestrain.

He was readmitted for further observation on Jan. 19, 1943. He appeared to have lost any neurasthenic aspect of his condition. He was sexually cold, but no longer impotent. He now had sparse black hair on the cranium, grey on the occiput and temples and on the pubes, chest and axillæ. There were no eyelashes or eyebrows. He shaved twice a week. His weight had remained steady. He got occasional headaches and attacks of giddiness, for which reason he had not returned to engine-driving.

DISCUSSION (R. G.)

My hair is grey, but not with years,
Nor grew it white
In a single night,
As men's have grown from sudden fears.

BYRON: *The Prisoner of Chillon.*

Hartley Coleridge records that the hair of Ludovico Sforza, the patron of Leonardo, became suddenly white from terror and Marie Antoinette's less rapidly from grief. The device has become one of the commonplaces of literature, which never, however, records whether alopecia totalis precedes the pigmentary change. That this omission may have been due to wilful suppression of an unromantic transitional phase is suggested by the frequency of the association in medical reports. Spiegler (1918), Stern (1922) and Pusey (1928) report alopecia and greying following emotional shock; Hurst (1940) mentions greying alone. In 1938, Thomson reported a case almost exactly similar to our own. After a very painful accident to his left hand, his patient lost all his hair (which afterwards grew white) and became wrinkled and old beyond his years. He lost weight and libido, and suffered from insomnia and headache. Investigations revealed a normal glucose-tolerance curve and a slightly low BMR. A fractional test-meal was refused. The blood-count showed 4,945,000 red cells per c.mm. and a hæmoglobin percentage of 88. Recovery was clearly taking place at the time of the report. Recently Allen and Carlyle-Gall (1942) reported a case in which almost total alopecia and loss of libido were associated with mental depression, but unfortunately the only laboratory investigations performed were an estimation of urinary androgens and the Wassermann reaction, both of which were normal. The suggestive point in their case was that the condition followed vaccination. Smith (1938) had already reported a case of total alopecia (followed by the growth of white hair), secondary hypogonadism, loss of weight and appetite, and polycythæmia following an acute undiagnosed pyrexial disease associated with an abdominal rash. It is tempting to associate both cases with encephalitis affecting the hypothalamus, though no positive evidence for this is available.

The points of similarity between these cases and Simmonds's disease need no stress. But Simmonds's disease is a condition of anterior panhypopituitarism, in which all functions of the anterior pituitary are diminished or suppressed. In no record of sudden senescence can so complete a syndrome be recognised. Moreover, though loss of pubic hair is characteristic of Simmonds's disease, total alopecia is not. The parallel is closer with the remarkable series presented by Snapper, Groen, Hunter and Witts (1937). Their six cases all showed excessive fatigue, evidence of thyroid deficiency, hypogonadism, anæmia and hypochlorhydria (in five cases complete achlorhydria). All suffered some degree of alopecia, though it was total only in case 1. In case 2, the disorder followed postpartum hæmorrhage and is similar to the cases of Simmonds's disease following parturition reported by Sheehan (1937, 1939, 1940; Sheehan and Murdoch 1938a, b). In case 3 there was a chromophobe adenoma of the pituitary. Only in these two is pituitary damage relatively certain, and in these the scalp hair was not lost. Pubic and axillary hair were absent in all six. That in all six cases anterior pituitary deficiency was present may be accepted. It was proved by the effects of trophic extracts in cases 4, 5, and 6, and in cases 2 and 3 may be assumed for the reasons already given. In case 1, the clinical examination leaves no room for doubt. That the pituitary deficiency was primary except in cases 2 and 3 is less certain. The symptoms of Simmonds's disease may be seen in lesions of the hypothalamus (Leschke 1933), and a vast literature has accumulated on the control by the hypothalamus of the whole endocrine system. Endocrine symptoms and signs have been reported in hypothalamic damage due to increased intracranial pressure, internal hydrocephalus, trauma, tumour, vascular disease, syphilis, and, most frequently of all, encephalitis. In such cases, achylia gastrica and anæmia are common.

It seems therefore probable that the cause of sudden senescence should be sought less in the pituitary gland than in the hypothalamus, an organ susceptible alike to the attacks of the virus of encephalitis and to the violent emotions of fear and pain. It is interesting to speculate on the extent to which such cases may provide a clue to the changes of normal senility.

SUMMARY

A case is recorded of total alopecia associated with lassitude, impotence, anæmia and achlorhydria developing in a man of 39 after a fall. A comparison is made with Simmonds's disease and the "anterior pituitary" syndrome of Snapper and others. The suggestion is made that the cause of premature old age should be sought in the hypothalamus rather than in the pituitary gland.

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PURPURA OF THE SKIN

A REVIEW OF 500 CASES

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CLASSIFICATIONS of purpura have often appeared, but they have generally been based on a search of hospital records (and of published work) rather than on personal experience. The incidence of the various types of purpura has had meagre attention, and it is not always clear what an author means by purpura. I have therefore reviewed 500 consecutive purpuric patients in each of whom I saw skin-purpura with or without other hæmorrhages. Those who bruised on trivial injury were not included unless they also had spontaneous ecchymoses or petechiæ. Purpura has been sought and repeated bruises without knocks inquired for routinely in practically all my patients since 1938. Many interested patients have referred relations to me, some of whom proved to have purpura. The 500 cases are analysed in the accompanying table.

ANALYSIS OF 500 CASES OF SKIN PURPURA

Group A.—183 cases (37%)	Cases	
Purpura simplex		78
Schönlein's purpura	12	14
Henoch's purpura	2	
Hereditary familial purpura simplex		79
Hæmorrhagic diathesis (pseudo-hæmophilia)		
Non-familial	4	7
Familial	3	
Primary thrombocytopenic purpura		4
Hæmophilia		1

Group B.—Symptomatic purpuras, 317 cases (63%)		
Physical		
(*a*) Cold	2	7
(*b*) Mechanical, Orthostatic	1	
Traumatic	4	
Chemical		
Gold	4	5
Sulphapyridine	1	
Bacterial disease		
(*a*) Acute	23	41
(*b*) Subacute	7	
(*c*) Chronic	11	
Virus disease (measles)		1
Spirochætal:		
Syphilis	6	9
Weil's disease	3	
Parasitic (trichiniasis; Davis and Allott 1941)		2
Cachectic and terminal		32
Purpura senilis		67
Scurvy		5

Group B (continued)	Cases	
Metabolic		
Diabetes mellitus	1	2
Hæmachromatosis	1	
Endocrine		
(*a*) Cushing's syndrome	7	14
(*b*) Menstruation	1	
Puerperium	2	
Pregnancy	3	
Menopause	1	
Dermatological		
Urticaria	3	7
Erythema nodosum (cause not found)	1	
Exfoliative dermatitis	2	
Disseminated lupus erythematosus	1	
Alimentary		
Peptic ulcer	1	3
Chronic cholecystitis	1	
Ulcerative colitis	1	
Cardiovascular		
Cardiac	23	49
Arterial	20	
Venous	6	
Nephritis (chronic)		7
Rheumatic		
Fibrositis	9	47
Rheumatic fever	7	
Rheumatoid arthritis	21	
Osteo-arthritis	9	
Acute gout	1	
Hæmatological		18
Neoplastic (meningioma of the spinal cord)		1

Purpura simplex.—The 78 cases included 72 females. Another 24 patients gave a convincing history of this condition but as I did not personally see their purpura they were excluded from the series. Among the 12 sufferers from Schönlein's purpura were 11 females.

Hereditary familial purpura simplex (Davis 1939, 1941).—I saw 79 cases (including 75 females) in 46 families. There were 51 additional cases in these families in whom the purpura was not personally confirmed.

Mechanical.—In one patient the upright posture was the chief factor inducing petechiæ of the legs but in 10 others this posture aggravated purpura from other causes. I have reported one of the traumatic cases (Davis 1940).

Bacterial diseases.—(*a*) The acute cases comprised 11 of meningococcal meningitis, 3 of tonsillitis, 2 cases each of pneumonia, (dry) pleurisy, and *Bacillus coli* pyelitis, and 1 case each of osteomyelitis, bacteræmic endocarditis, and bronchitis. (*b*) The subacute cases included 4 of infective endocarditis and 3 of pyogenic abscess. (*c*) The chronic cases were 3 each of pulmonary tuberculosis and bronchitis, 2 each of sepsis and cystitis, and 1 of bronchiectasis.

Syphilis.—There were 3 meningovascular cases, 2 of aneurysm of aorta, and one tertiary.

Cachectic and terminal.—This group comprised those who were dying, usually from chronic disease, and purpura first appeared a few days or hours before death. There were 14 cases of cancer, 5 of senile bronchopneumonia, 5 of pulmonary tuberculosis, 4 of terminal congestive cardiac failure, 2 of uræmia and 1 case each of strangulated hernia and terminal meningovascular syphilis.

Scurvy.—Two cases were seen before the war, and 3 since (Davis 1942).

Cushing's syndrome.—Of 10 cases seen since this inquiry began 7 had skin-purpura.

Urticaria.—In 3 cases, purpura and urticaria were present together. One patient showed petechiæ at the periphery of the actual urticarial lesions.

Cardiovascular.—(*a*) Cardiac: 19 cases of congestive cardiac failure, 2 of left ventricular failure, and 1 each of angina pectoris and myocardial infarction. Of those with congestive heart-failure 7 showed gross purpura, 2 of these having the most extensive skin involvement of the series of 500. It was found that petechiæ and ecchymoses not uncommonly appeared over œdematous areas and not only in cardiac œdema.

(*b*) Arterial: 7 cases of cerebral thrombosis, 3 each of cerebral hæmorrhage, general arteriosclerosis, malignant hypertension and hypertensive encephalopathy; and 1 of high blood-pressure.

(*c*) Venous: 5 cases of varicose veins and 1 of thrombophlebitis.

Rheumatic diseases.—It was found that 8 of each of the 9 patients with fibrositis and osteo-arthritis were females, and that all my cases of purpura in rheumatic fever and rheumatoid arthritis were females. Of the 7 cases of rheumatic fever, in 4 the purpura accompanied the acute attack and in 3 purpura began within one year of onset of the disease (see Davis 1940).

Blood diseases.—These comprised 8 cases of addisonian anæmia, 4 of leukæmia, 2 of aplastic anæmic, and 1 case each of simple achlorhydric anæmia and hæmolytic disease of the newborn. There were also 2 cases of Hodgkin's disease.

Vitamin K.—Prothrombin estimations were not done in the series reported. Jaundice was seen in some of the patients with cancer, congestive cardiac failure and blood disease; while in addition to the patient listed with chronic cholecystitis and purpura, 9 others in this series had gall-bladder disease.

Capillary microscopy.—For some eighteen months I have examined the nail-bed capillaries of many patients with purpura. In purpura simplex it is not uncommon to see microscopic blood extravasations from these capillaries.

DISCUSSION

The degree of purpura in these cases varied from a few petechiæ to the involvement of the greater part of the skin. Ages ranged from a few hours to 89 years. In the rheumatic purpuras females were mostly affected, and purpura simplex (familial and non-familial) was overwhelmingly more common in women.

Förster (1878) reported 60 cases of purpura in 83,000 children and stated that Scheby-Buch found 174 cases in 100,000 patients in 41 years in Hamburg. Purpura in London is evidently far more common, for the 500 cases were seen in 50 months.

If it is true that vitamin P exists in citrus fruits and that this vitamin is essential for normal capillary resistance, an increase in purpura might be expected in current war-time conditions. So far I have not seen any increase.

Useful recent classifications of purpura have been given by Peck and his colleagues (1937), Forkner (1938), and (a remarkably comprehensive one) by Jürgens (1941). Haden and Schneider (1941) described 310 cases "studied completely" for hæmorrhagic disease. Perlman and Fox (1941), reviewing autopsy reports, found 355 cases with evidence of hæmorrhagic diathesis in 10,355 autopsies. Their information is of value, but it must be noted that these workers regarded as a hæmorrhagic diathesis any extravasation of blood through the endothelial walls of capillaries, external or internal, regardless of amount; and that cases of benign purpura rarely reach morbid anatomists.

Anaphylactoid purpura.—This conception has intrigued hæmatologists, many of whom include purpura simplex, and Schönlein-Henoch purpura under this term. Yet in

only a minority can an allergic cause of these purpuras be demonstrated as in Hampton's (1941) 2 cases. There is as yet quite inadequate evidence for regarding most of these purpuras as allergic. Of my 78 cases of purpura simplex, in 8 there was a significant history of urticaria, in 8 others purpura began in the wake of an acute infection and 15 had suffered from rheumatic fever. Of the 79 cases of hereditary familial purpura simplex 23 had had rheumatic fever. In my own series the rheumatic diathesis was more important than allergy (unless the rheumatic diathesis is itself regarded as allergic) and clearly there are other factors to consider. To classify this group as a whole as anaphylactoid is unwarranted at present.

Purpura and rheumatism.—I have previously given evidence of a special association between purpura simplex and rheumatism (Davis 1941). It is well known that rheumatic features may be seen in patients with purpura, but it is insufficiently known that if purpura is sought for among the various "rheumatic" sufferers, it will be found fairly commonly, particularly among the women. This striking sex association (found also in purpura simplex) presumably has an endocrine basis.

In any one patient multiple factors may contribute to purpura, e.g., two or more of the following: rheumatism, the menopause (Davis 1939), other endocrine factors, infection, œdema, and orthostasis. But in the table each patient has been allotted to a single category only—that judged to be the most important. The symptomatic purpuras were in a clear majority. Benign purpura was very common, particularly purpura simplex (familial and non-familial), and the serious purpuras were relatively rare. Tidy (1926, 1937) was unnecessarily pessimistic when he stated that purpura should never be regarded lightly. He considered purpura simplex and purpura hæmorrhagica to be grades of severity of the same condition but only rarely did any of my patients with purpura simplex develop serious hæmorrhages (Davis 1941). I have stressed (Davis 1939) some familial associations of hereditary purpura simplex (e.g. rheumatism, tuberculosis) but the prognosis in purpura simplex is almost invariably good. As regards symptomatic purpuras, a few crops of petechiæ in the course of an acute infection did not of itself affect the outcome, though the appearance of extensive purpura was often (but by no means always) of grave import. In some of the most extensive purpuras seen, the patient recovered completely.

SUMMARY

A series of 500 consecutive cases of skin-purpura is analysed.

Symptomatic purpuras formed 63% of the series.

Benign purpuras were in a majority and serious purpuras rare.

The connexion between purpura and rheumatism is stressed.

There was no war-time increase in purpura.

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EMERGENCY TREATMENT OF THE SMASHED-IN FACE

VALUE OF TRACHEOTOMY AND LARYNGOTOMY

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THE smashed-in face resulting from a severe blunt external force is emerging as a clinical entity. With the motor-car and aeroplane as common agents in its production it is essentially an injury of modern civilisation. But it may also be produced in other ways. Thus we have seen cases : resulting from a fall down a flight of stone steps on to the face ; in a cat burglar whose judgment on the security of the outside piping of the second storey was deficient ; and in a workman engaged in digging up the road with a mechanical drill which flew back in his face. We have also seen an example in an air-raid casualty where severe injuries were caused by falling masonry, and our colleague, Major P. B. Ascroft, met with cases in the Western Desert, again resulting from various types of blunt force rather than from missiles. The increasing incidence of this and allied injuries and the problems arising in their treatment have led during the war to the establishment of special faciomaxillary units, and the results of the special studies in these units are now beginning to flow back to strengthen and enrich the main stream of surgical progress. But in the stress which is rightly laid on the importance of the early transference of these cases to a faciomaxillary unit and in the illustration and description of the various technical methods which may there be employed, it has tended to be overlooked that they have also an emergency aspect which, if not satisfactorily solved, may prevent them ever reaching the special unit. Having experienced the difficulties which are encountered in the immediate management of these cases we venture to give the conclusions to which we have come on their treatment by the emergency surgeon.

Taking a typical severe case, a patient having sustained a severe blunt injury to the face is admitted with the face swollen and distorted, and in parts depressed. There are lacerations of the skin and superficial soft tissues, with perhaps some of the soft tissues torn back in the form of flaps. The patient's face is covered with dirt and with blood, which is also both dripping out from the nose and mouth and running back into his pharynx ; this makes him cough and splutter, and also interferes with the freedom of his airway, so that he may have difficulty with breathing and be cyanosed—which again tends to increase the amount of bleeding. He may be unable to open his eyes owing to swelling of the eyelids. Various bony injuries may be obvious to inspection : the frontal sinus may be driven in, the nose crushed, the upper or lower jaws fractured, the alveolar margins distorted and teeth loosened or detached. He may show general signs of shock and loss of blood.

Kilner [1] has pointed out the importance in the first-aid treatment of these cases of turning the patient on to his side so that blood can run forwards and the respiratory embarrassment thus be prevented, and the Medical Manual of the American Army [2] also gives valuable first-aid hints. On admission to an emergency surgical unit, the first step is clearly the control of hæmorrhage and a primary approximation of the soft tissues and fractured bones. But at once the difficulty of anæthesia presents itself. Intratracheal anæsthesia is the ideal, but the preliminary phase of inhalation anæsthesia through a facial mask is difficult not only because of the facial injuries but, more important still, because of the blood which is constantly running into the pharynx and leading to coughing and partial obstruction. And if the patient is, in spite of the difficulties, successfully anæsthetised past the stage of the cough reflex, he tends to aspirate the blood into his lungs and may drown in his own blood. We have each had examples of this recently, the patients only being saved from death from asphyxia by a rapid tracheotomy, after which they at

1. Kilner, T. P. *Med. Pr.* 1941, **205**, 26.
2. National Research Council. Manual of standard practice of Plastic and Maxillo-Facial Surgery, Philadelphia, 1942.

once coughed considerable amounts of blood back through the tracheotomy tube. At first sight intravenous anæsthesia by pentothal might be thought to solve the difficulties, but Major Ascroft tells us that he had a case in which asphyxial symptoms developed so quickly after intravenous injection that the patient's life was only saved by a rapid plunge laryngotomy and it would seem that the respiratory depressant effect of the usual intravenous anæsthetics is an additional disadvantage. In view of these experiences, therefore, we suggest that the standard initial emergency treatment of the severe types of smashed-in face as described above should be tracheotomy or laryngotomy under local anæsthesia. Once an opening into the air passages has been made, the anæsthetic problem becomes easy, the danger of death from asphyxia is averted, the reduction in cyanosis from the establishment of a free airway may by itself result in cessation of much of the hæmorrhage, and the surgeon can if necessary proceed to further measures for the local control of hæmorrhage, the approximation of the soft tissues, and the correction of gross bony displacement.

The essential task of the emergency surgeon is now finished, and it remains only for him to dispose of the case for its final treatment. In most cases this means its early transfer to a special faciomaxillary unit. But there may be emergency aspects other than those he has successfully dealt with. In the first place, the eyes may be damaged; one of our cases had a ruptured globe and bilateral retinal detachment and was rendered almost totally blind. The damage to the eyes may be concealed by the swollen eyelids. A deliberate inspection of both eyes by the gentle insertion of small retractors under the swollen lids and, in any case of doubt, an immediate opinion from an ophthalmic surgeon would therefore seem to be an essential duty of the emergency surgeon. Secondly he should bear in mind the possibility of cerebrospinal rhinorrhœa and the cerebral surgeon's interest in getting cases with this complication early. And, finally, the routine administration of one of the sulphonamides may be valuable in preventing aspiration pneumonia and local sepsis.

CONCLUSIONS

The severely smashed-in face is a clinical entity with clearcut emergency features.

In difficult cases emergency tracheotomy or laryngotomy may be life-saving.

The duties of the emergency surgeon in these cases are: (*a*) to deal with hæmorrhage and gross soft-tissue and bony damage; (*b*) to inspect the eyes and, if necessary, to secure the coöperation of the ophthalmic surgeon; (*c*) to be on the look-out for any suggestion of cerebrospinal rhinorrhœa; (*d*) to administer prophylactic sulphonamides.

Having completed the emergency treatment, early transfer to a special faciomaxillary unit should be arranged.

Diagnostic X rays have little place in the emergency treatment of these cases, and time should not be wasted in trying to obtain them.

Reviews of Books

Ear, Nose and Throat in the Services

R. SCOTT STEVENSON, MD EDIN, FRCSE, major RAMC. (Humphrey Milford, Oxford University Press. Pp. 116. 5*s*.)

THIS book is really an elementary primer on ENT disease, with here and there an allusion to Service—chiefly Army—problems. It is intended for "the average medical officer" in the various services (which makes it the more regrettable that so much space should be given to tracheotomy (after the author has stated that it should never be done except as a set formal procedure), submucous resection of the septum and tonsillectomy. Qualified ENT surgeons are employed by all the Services for hospital work, and are by definition familiar with the more simple operations. The medical officer in the Services has the same sort of ENT problems to face as a general practitioner in civil life—it is the disposal, not the treatment, of these cases that presents difficulties. In the Army, men with active chronic middle-ear suppuration (who should never have been passed fit by the medical boards) are retained and treated, and even have radical mastoidectomy done. In the RAF, these men are generally invalided out, unless they have been overlooked sufficiently long for them to have acquired trades, or unless they are trained permanent staff. Radical mastoidectomy is only performed if urgent symptoms make it necessary. Airmen are regarded as unfit for overseas duty if they have a perforation in either drum, whether or not the middle ear is moist or dry. But these, and certain minor discrepancies, will not affect the average MO's pleasure in rubbing up his knowledge of upper respiratory tract disease in an entertainingly written manual.

Notes for the RMO of an Infantry Unit

C. P. BLACKER, MC, MA, DM OXFD, FRCP, late RMO, 2nd Batt. Coldstream Guards. (Oxford Univ. Press. Pp. 77. 5*s*.)

Dr. Blacker has had three years' experience as a regimental medical officer in the present war; he served as a combatant officer in the last. Obviously he knows how to pick good men. Having done so, he trains them to shoulder responsibility and to show initiative in routine duties, thereby increasing their capacity to cope with an emergency. Some of his own methods of dealing with the problems confronting a regimental medical officer are original; all are practical—for example, his method of tackling venereal disease. He holds the view that continence is more usual among soldiers than is generally supposed. But for the few he provided condoms in preference to emergency treatment packets, which, with their complicated ritual, are not popular, and not very practical for men who may not be quite sober. The condoms, bought through a loan from the CO's fund, were retailed at a small profit by the senior stretcher-bearer in each company, who was thus provided with "a simple exercise in keeping accounts"; and the arrangement gave reasonable privacy to the buyer. The profits—consumption was not heavy—went into a small regimental aid-post fund. Throughout the book the author looks at his work from other angles than his own; he appreciates the viewpoint of the ADMS, of the company officer, and most of all of the men under his care. Even experienced RMOs will pick up useful wrinkles, and those newly appointed will find help on every page.

Essentials of General Anæsthesia

(3rd ed.) R. R. MACINTOSH, DM OXFD, FRCSE, DA; FREDA BANNISTER, MD LPOOL, DA. (Blackwell. Pp. 341. 16*s*.)

WRITTEN for senior students, there is much in this well-established book to interest anæsthetic specialist. The chief difference between this edition and the last is the addition of a chapter on the Oxford vaporiser, where happily there has not been the usual lag between scientific conception and practical applications. Although complete where dental operations are concerned, more guidance would be welcome in the management of special operations on other regions, such as the thyroid, the abdomen and the brain. As it stands, the book remains an excellent exposition of the general principles of anæsthesia and the illustrations are of a very high order.

Urology in War

CHARLES Y. BIDGOOD, lieut.-commander (MC) USNR, chief urologist, U.S. Naval Hospital, Washington, DC. (Baillière. Pp. 78. 11*s*.)

IN this authoritative little book Commander Bidgood describes the treatment of genito-urinary lesions in a well-equipped military hospital. He does not tell the reader about the treatment of war wounds of the genito-urinary tract, and how these wounds should be handled during the journey from the front to the base hospital; and he says nothing about the various types of wound that will be met with or of the damage inflicted by different varieties of missle. To this extent the author does not achieve his aim of providing a book "to serve as a reference for officers aboard ship or in isolated outposts who may be confronted by such emergencies and forced to ope with them." But it will be useful to general surgeons working at the base who have had only limited urological experience.

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THE LANCET

LONDON: SATURDAY, AUGUST 7, 1943

TOXINS AND SHOCK

THE story of shock is still far from complete. Interest in it rises and falls with the wars that seem to be part of our destiny. In 1918, after four years of intensive investigation, a conclusion had apparently been reached. The work of DALE, LAIDLAW and RICHARDS, and CANNON and BAYLISS, had provided evidence that a toxic substance (or substances) was formed in injured muscle, and that this was absorbed into the general circulation, where it induced widespread capillary damage with leakage of plasma into the tissues: thus the reduced blood volume and hæmoconcentration reported in casualties from France were explained. With this theory of traumatic toxæmia the word histamine was commonly associated; but the originators of the theory, though they emphasised the similarity between histamine poisoning and shock, did not claim that the two were identical. It was later realised that skeletal muscle is relatively poor in histamine and could not produce enough to account for the circulatory changes in shock; increased quantities of histamine, moreover, could not be found in the blood of injured animals. This failure to incriminate histamine tended to discredit the idea of traumatic toxæmia. MOON maintained his faith in the reality of an elusive toxin or toxins, but most other workers focused their attention on BLALOCK'S explanation of shock in terms of fluid loss at the site of injury, and on O'SHAUGHNESSY and SLOME'S revised theory of nervous exhaustion.

With the outbreak of the present war, research was again intensified. It became evident that we had fallen into the habit of thinking of only one factor as the cause of shock, whereas probably there are several acting at the same time. Thus the various hypotheses already mentioned may each furnish part of the answer. While BLALOCK was able to demonstrate that local fluid loss was sufficient in most of his experiments to kill his animals, there were instances in which some other factor seemed to be operating. Similarly WILSON and ROOME were satisfied that death following the removal of a tourniquet which had been applied to a limb for several hours could usually be explained by the leakage of plasma into the limb from the capillaries damaged during the period of ischæmia; but they found that amputation of the limb at the level of constriction, and the transfusion of blood or plasma, did not always save the animal as might have been expected.

Elsewhere in this issue, GREEN, and BIELSCHOWSKY and GREEN, report observations on limb ischæmia in a number of different species. They set out to investigate the crush syndrome by producing hind-limb ischæmia, but were led by their preliminary results into a renewed search for the muscle toxin postulated by DALE, CANNON and BAYLISS after the last war. Their experiments have been laborious and tedious, and at times must have been disheartening; the apprehension of a toxin has been bitterly compared with the mapping of an amorphous dung-heap. Nevertheless, by patient endeavour they have been able to show that an extract (muscle shock factor, MSF) can be obtained from skeletal muscle which will reproduce on injection the signs and symptoms that follow removal of a tourniquet from an ischæmic limb. Further analysis of this purified extract has revealed that the greater part of its activity is probably attributable to adenosine triphosphate. Like limb ischæmia—though not to the same extent—MSF causes depression of renal function with uræmia and raised non-protein nitrogen; in about a quarter of the animals that survive, the urine contains albumin, granular casts and red cells, and occasionally there is frank hæmaturia. The histological changes in the kidneys are not great, but combined injection of myohæmoglobin and MSF will produce definite renal damage—dilatation of the second convoluted and other tubules, with amorphous brownish-yellow casts in large numbers. Before the significance of MSF can be properly assessed it will have to be proved that the condition following its injection is identical with the condition following limb ischæmia. It must be shown either that the blood or tissues of the animal suffering from limb ischæmia contain MSF in substantially greater quantities than are found in any other morbid state or in the normal animal, or else that MSF can be used to immunise the body against shock. The substance is destroyed in the tissues so rapidly that the first of these alternatives will probably be hard to achieve; and experiments designed to prove the other have so far been unsuccessful. The instability of MSF probably explains the lack of success of previous seekers for a muscle toxin.

Though much remains to be done before MSF can be held responsible for any of the effects of tissue damage in animals—let alone in man—GREEN and BIELSCHOWSKY have made a valuable contribution to a difficult and very important problem. Their isolation of a chemical substance is in itself a great advance.

CALIBRATING THE PELVIC CANAL

OBSTETRICIANS as a class are becoming X-ray conscious, and are ever more calling on the radiologist to help in detecting cephalopelvic disproportion. There is perhaps no harder task. The pregnant woman is fat, broad and deep, and pictures of good quality are difficult to get. Long exposures are necessary, and equipment must be carefully nursed if it is to stand up to this heavy work. In normal times a tube replacement may mean a bill of £50; nowadays more than money is required to make good its loss. For these reasons radiograms should be asked for only when some clear purpose is in view and clinical examination has failed to give adequate guidance. Much ingenuity has been shown in devising methods by which the magnified, and sometimes distorted, shadows of the pelvis can be made to show the true pelvic size and form. For routine work the technique must not be difficult or complicated, and reading the results must not be unduly time-consuming. Ideally, the radiogram should show the anteroposterior diameter of the pelvic brim (the conjugata vera); the anteroposterior diameter of the lower pelvis (pubosacral); the transverse diameter of the brim; the distance between the ischial spines; and the size of the pubic arch. In addition, it should enable some estimate to be made of the size of the fœtal head, and if possible should supply a measure-

ment of its biparietal diameter. These requirements are exacting enough, but their attainment serves only to set a new problem—the interpretation to put on the various measurements obtained. The difficulties are many. Errors of technique tend to exaggerate the size of the fœtal head and minimise the size of the pelvis. Absolute measurements are less important than relative measurements, and the pelvis as a whole must always be considered rather than the size of one particular dimension. There is a tendency for the inexperienced worker to take an unnecessarily gloomy view of supposed disproportion.

ROHAN WILLIAMS [1] urges the routine use of a two-plane projection of the pelvis. From pictures so obtained the pelvic size and shape can be reproduced in outline form on paper. An ellipse, representing the estimated size of the fœtal head, is cut from a piece of paper and manœuvred through the artificial pelvis. Disproportion, if present, is then readily estimated. Somewhat similar methods have been described by THOMS [2] and by MOIR.[3] WILLIAMS shows pelvimetry tracings of 22 cases and gives details of the clinical course of labour in 13 that were classed as "borderline." In 7 of these the radiological forecast was later justified, in 3 cases the prognosis had been non-committal, and in 3 others the prognosis made was later proved wrong. These examples include early cases, and with increased experience some of the errors would have been avoided. MOIR [4] uses three views of the pelvis—a lateral radiogram, a "plan" view of the brim obtained with the patient in the reclining position, and a view of the pubic arch. He thinks the lateral view the most important. This is obtained with the woman standing up. By a simple arrangement of wooden pegs, against which the patient presses her anterior superior spines, a true lateral position is easily secured, and the patient kept motionless during the exposure. MOIR discusses such complicating factors as head moulding and the rate of head growth. Moulding is relatively easy and safe in a small fœtus but more difficult and dangerous in a large postmature fœtus with a well-ossified head. Pelvic shape is important as well as size. Thus, prognosis is more favourable with a pelvis deformed by rickets than with a generally contracted pelvis with a brim conjugate of the same size. This was exemplified in 2 cases in which the conjugate measured 3½ and 3¾ in.; vaginal delivery was relatively easy in the first but impossible in the second. Radiography is thus of value in revealing pelvic type, as well as in showing the precise dimensions, such as the traditionally honoured conjugate of the brim. Radiography is especially useful in breech presentation, where the clinical test of gauging the head against the pelvic brim is not available. In assessing pelvic disproportion charts are used to show pelvic shape and capacity in relation to head size. NICHOLSON [5] has studied the pelvic capacity of healthy women in a rural district of England, and a somewhat similar investigation has been made in London by INCE and YOUNG.[6] Some textbook statements regarding pelvic size will have to be revised in the light of the new facts now established. NICHOLSON assesses disproportion by calculating the area of the pelvic canal at the brim and at the level of the ischial spines. He visualises the moulded fœtal head as a circle, the cross-section area of which he reckons in terms of the biparietal diameter. For easy delivery he believes that the area of the head so calculated should not exceed 80% of the area of the brim. In the lower pelvic plane the limit of safety is probably considerably higher. NICHOLSON [7] also expresses his findings in another form. Having regard to the incidence of the different sizes of fœtal heads at term, he concludes that a pelvis with an area of 110 sq. cm. at the brim can pass 99·9% of all fœtal heads; a pelvis of 100 sq. cm. can pass 97%; a pelvis of 90 sq. cm. can pass 70%; while a pelvis of 80 sq. cm. can pass only 21% of all fœtal heads. Similar calculations have not yet been made for contractions in the lower pelvis.

It is wrong to suppose that the radiologist can now supplant the clinician in deciding the best treatment in doubtful cases of obstetric disproportion. Indeed, the problems involved are so complicated that it is doubtful if he ever will. Nevertheless, in some directions radiography can give information more precise than that obtained by usual clinical methods, and can thus help to bridge the gap sometimes left by these methods. Thus far radiologists and obstetricians have been feeling their way. Soon a firmer guidance can be expected, and with it will come a clearer understanding of the scope and limitations of pelvic and of cephalic mensuration.

1. Williams, E. R. *Brit. J. Radiol.* 1943, **16**, 173.
2. Thoms, H. *Amer. J. Surg.* 1937, **35**, 372.
3. Moir, J. C. *Edinb. med. J.* 1941, **48**, 361.
4. *Proc. R. Soc. Med.* 1943, **36**, 359.
5. Nicholson, C. *J. Obstet. Gynæc.* 1938, **45**, 950.
6. Ince, J. G. H. and Young, M. *Ibid*, 1940, **47**, 130.

MEDITERRANEAN ANÆMIA

THE name of COOLEY is associated with a severe anæmia that affects children of parents of Mediterranean stock. Its characteristic features are well-marked hypochromic anæmia with numerous normoblasts in the blood, enlargement of the spleen and sometimes of the liver, a mongoloid facies, osteoporosis with peculiar X-ray appearances, especially in the skull, which shows a perpendicular striation of the diploë, and decreased fragility of the erythrocytes; the disease is familial, few children survive much beyond their first decade; iron, liver, and splenectomy have all been tried without effect. It is now realised that this syndrome represents the severest form of a widespread hereditary hæmopoietic disease and that there is a whole series of cases ranging from this severe form to non-anæmic persons in whom some of the typical blood changes can still be found. An analogous series is already known in the group of cases called familial acholuric jaundice; in this disease there is increased fragility of the erythrocytes and blood-films show small densely staining microcytes known as spherocytes. These spherocytes and sometimes increased fragility, sufficient to be detected by our rather crude methods, have been found in the apparently unaffected relatives of patients with frank acholuric jaundice, and investigations of this sort have helped in establishing the familial nature of the disease. In Mediterranean anæmia there is decreased erythrocyte fragility and the peculiar cell seen in blood-films is the unusually thin red cell that shows up sometimes as a "target cell"—a cell with a dense central spot in an otherwise pale interior—sometimes as a hypochromic but large cell.

By searching for these abnormal cells and testing

7. Nicholson, C. *Biometrika*, 1941, **32**, 16.

the red-cell fragilities in relatives of cases of Cooley's anæmia, it has been found that the syndrome is actually very widespread in its mild forms and that there is a definite hereditary basis for it. CAMPINOMETROS,[1] working in Sicily, thought that there might be a Mendelian recessive mode of inheritance. DAMESHEK,[2] who has recently described a further series, is less dogmatic, but finds the target-cell syndrome present in both parents and certain siblings of cases of Cooley's anæmia. Van RAVENSWAAY, SCHNEPP and MOORE[3] have described a case in a Greek patient who had reached the age of 34; out of his 4 children, 3 had died of Cooley's anæmia and there is suggestive evidence that his parents' families were widely affected. SMITH[4] of New York investigated 16 families in whom children had developed classical Cooley's disease or a moderate but refractory anæmia; out of 63 persons, blood changes typical of Mediterranean anæmia were found in 54. SMITH regards the decreased fragility to hypotonic saline as the most useful single test and points out that, though target cells were only found in half his cases, all except one had decreased fragility and their blood-films showed other evidence of the presence of thin cells such as hypochromic polychromatic macrocytes—an unusual combination. The sternal marrow showed normoblastic hyperplasia with the same red-cell abnormalities as the peripheral blood. SMITH is in no doubt about the hereditary nature of the disease and points out that a mildly affected patient may have severely affected children; but he has not sufficient evidence to determine the exact mechanism. The mild cases seem to live normally without inconvenience; for the others no treatment has had any effect—iron, liver extracts, vitamin-B complex in various forms are no use; splenectomy makes them worse. A severe anæmic episode or an intercurrent infection is the normal termination. Van RAVENSWAAY'S patient described a local Greek method of treatment that he had himself experienced; it consisted in a primitive form of wet-cupping, with pressure on the spleen applied by hooking the edge of the enlarged organ over the top of a fence and then hanging suspended with both feet off the ground.

In the Mediterranean area the most important differential diagnosis is from chronic malaria. The combination of chills, fever and splenomegaly occurs in both, and van RAVENSWAAY quotes a statement from a Greek source about "hereditary malaria"; were these really cases of Mediterranean anæmia and would target cells have been found in their blood if they had been looked for? It is notable that most of the observations on Mediterranean anæmia have been made on persons born in Italy, Greece or Syria and their children who had emigrated to the USA; records from the Mediterranean countries themselves are few. These countries are now much in the news and the time may be near when relief measures among their debilitated populations, many of them anæmic, will have to be undertaken. To the common causes of malnutrition and malaria, it will be well to add this Mediterranean anæmia syndrome. We do not know how widespread it really is, but the characteristic red-cell changes are not difficult to detect even if fragility tests are impracticable in the field, and we do know that it is refractory to treatment; a search for these features in the blood of patients not responding to antianæmic or antimalarial treatment may give us new knowledge of this syndrome, and prevent mistakes in assessing the value of these treatments.

1. Campinometros, J. *Ann. Méd.* 1938, **43**, 27 and 104.
2. Dameshek, W. *Amer. J. med. Sci.* 1943, **205**, 643.
3. Van Ravenswaay, A. C., Schnepp, K. H. and Moore, C. *J. Amer. med. Ass.* 1943, **122**, 83.
4. Smith, C. *J. Amer. J. Dis. Child.* 1943, **65**, 681.

Annotations

COLLECTION OF CASUALTIES

IN the British Army each battalion or equivalent unit has a regimental medical officer. In the ordinary way the RMO is the sole representative of the RAMC attached to the unit, and he must find his assistants from its strength: thus his orderlies, NCOs and stretcher-bearers may be infantrymen, sappers or gunners, trained in first aid, but they are seldom members of his own corps. The United States Army works on the opposite principle. An American regiment, which corresponds to our brigade, normally has its own regimental medical detachment from the Medical and Dental Corps, and this is divided so that each battalion has a substantial medical section, comprising officers, NCOs, and other "medical soldiers." The arrangements are such that every platoon has the services of a trained orderly from the Medical Corps who accompanies it into action. The Americans like this system because there is never any question of reducing the fire-power of combatant units by assigning combatant personnel to medical duties; because training as a combatant is not wasted on someone who will be stretcher-bearing; and because they think their litter-bearer, as they call him, will be better trained if he is trained exclusively for his medical task.[1] The arguments in favour of the British system need not be stated here; but it must be admitted that the regular provision of medical personnel for our troops is on a less generous scale.

The Americans have lately described their routine for picking up wounded.[2] Each man carries, fastened to his belt, a first-aid package and a package containing sulphadiazine in tablets and powder. If conscious and able to do so, he is expected to dust the powder into his wound, apply his field dressing, and take the tablets by mouth. "In all probability, however, a hospital corpsman has reached him before he has a chance to do this." This hospital corpsman is the aid-man of his platoon, whose job it is to give urgent first aid, including an injection to stop pain. "He does not remain with the fallen soldier, as he has to move forward with the attack. After treatment he ties a tag to the soldier's belt telling what type of treatment was administered, fixes a bit of gauze to a bayonet or stick to mark the place where the soldier is, and goes ahead. Now come the litter-bearers, attracted by the white cloth"; and the patient is taken to the battalion or regimental aid station, where he may be given a transfusion of plasma, and is made ready for the first stages of his journey to the base.

Picking up casualties, however, is not always as easy as it may seem. Compared with his predecessor on the Western Front in 1914–18, the stretcher-bearer today has less to fear from mud, and is helped both by wireless information and by an abundance of motor transport. Indeed, he may become almost superfluous where a vehicle can be taken to the patient instead of taking the patient to a vehicle; and this has generally been possible in the recent North African campaign. On the other hand, the rapid movement of mechanised units means that casualties may be scattered over wide areas, and during contact with the enemy the troops may be unable

1. *Army med. Dept. Bull.*, No. 19, January 1943.
2. Report on Recovery of American Wounded. U.S. Office of War Information. May, 1943.

to spare time even to apply field dressings to their wounded comrades. In considering these factors Major Murray [3] concludes that stretcher-bearers must be disposed so as to provide immediate and essential first-aid, and he has devised a battle-drill for them which reduces searching to a fine art. The squads are trained to make systematic hunts in fields, scrub, woods and houses. During the search each bearer works singly, and when he finds a casualty his duty is merely to stop hæmorrhage and mark the man's position so that this can readily be found again. The squad then re-forms, and, where necessary, removes the wounded in turn to the most accessible place at which they can be transferred to motor transport. As became customary in Civil Defence work during air-raids, first aid on the spot is reduced to a minimum, being mostly left until the patient is in a vehicle. When accompanying troops in action, the bearers must practise fieldcraft and personal camouflage; for they must never be responsible for giving the unit's position away to the enemy. And skill is also called for in "medical fieldcraft"—the approach to, and removal of, the wounded man under fire both by day and by night. In urging the importance of this side of medical work in the field, Murray demonstrates that it often needs a trained mind in a trained body; but undoubtedly motor transport has lightened the physical burden on the stretcher-bearer, and very often it can take his place.

ETHICS FOR THE YOUNG PRACTITIONER

In an address to Guy's students, Sir Herbert Eason [4] has summarised the standards of professional ethics with the authority of the president of the tribunal responsible for their enforcement. Mention of the Warning Notice issued by the GMC naturally led him to an early reference to the risks of lax certification. He had been appalled, he said, in his hospital experience, to see house-officers signing certificates in blank for sisters or nurses or dressers to fill up afterwards—statements that the patient was suffering from some disability or disease and was unfit to follow his or her employment. He advised students never to sign a blank certificate or any document for the entire accuracy of which they were unable to vouch. "It is no good saying 'I have today examined So-and-so' when in fact you examined him yesterday." Next he expounded the warning against assisting unqualified practitioners. This was "infamous conduct" because it traversed the whole aim of the Medical Acts by obscuring the statutory distinction between the qualified and the unqualified. Administering an anæsthetic to help an osteopath's treatment of patients was covering an unqualified practitioner. But this did not mean that the qualified man cannot ask a masseuse to massage a patient. "You can even ask an osteopath or a chiropractor to assist you in treating a patient so long as the patient is under your own care." Of four other classes of conduct often brought to the notice of the GMC the commonest was that of the practitioner found drunk. The council, explained Sir Herbert, seldom takes a man off the Register for a single conviction of drunkenness; it will give him a warning. A second conviction for drunkenness probably means a stiffer warning. A third is likely to involve action. If a doctor habitually gets drunk, can he be fit to be in charge of patients? It is, of course, a grave matter to remove a man from the Register for three cases of drunkenness. The council may perhaps suspend judgment and put the respondent on probation for a year or so, requiring certificates as to his behaviour in the interval and insisting on an undertaking for good behaviour in future. Drunkenness in charge of a motor-car is more seriously regarded. It shows not only over-indulgence in alcohol but also a reprehensible absence of responsibility. A man who, when under the influence of alcohol, thinks himself fit to drive a dangerous machine like a car is a menace both to his patients and to the public. The other three classes of professional misconduct were described as the three As—advertising, abortion and adultery. The first includes those flattering little paragraphs about the distinguished surgeon or eminent physician and his well-known patients—laudation which a few practitioners signally fail to avoid, to the detriment of their more honourable and reticent brethren. The second, abortion, is, as the law stands, a felony punishable with penal servitude. Whatever views practitioners may hold about birth control, whatever appeals may be made to them to save an innocent's girl's reputation and her family's credit and social standing, they must realise that the GMC cannot ignore what the state regards as a serious crime. Lastly, a charge of adultery means that the council, without pretending to be a court of morals, must protect the public. Adultery per se is not infamous conduct in a professional respect, but, if committed with a patient or a member of a patient's household, it is a breach of trust and an abuse of confidence. To his admirable exposition of the professional code, and his virile statement of the things which are "not done," Sir Herbert Eason added two precepts of worldly wisdom. The practitioner who is charged in the police-court with drunkenness or other offences should never allow himself to be persuaded to plead guilty by the argument that he will thus escape publicity. Secondly, as soon as he is qualified, he should join one of the well-established medical defence societies. This will protect him from the formidable risks of practice, whether they arise from the accusations of female patients or from any other source. It will ensure for him legal advice and assistance from the day of his registration to the day of his retirement, amid unforeseen dangers which even the greatest care can hardly avoid.

CONTINUOUS SPINAL ANÆSTHESIA

The continuous technique frees spinal anæsthesia from the disadvantages of single-dose administration; and though the minimum dose which must be given for abdominal anæsthesia will allow sufficient operating time for most cases there are occasions when a chance to lengthen anæsthesia is welcome. The method will therefore apply chiefly to operations lasting longer than 1–2 hours. In the last few years, though simpler and safer methods have been developing, spinal anæsthesia has once again suffered from the enthusiasm of its new recruits, and those contemplating using the continuous method should take to heart Nosworthy's advice, quoted by Lee (p. 156), to learn the old technique first and then the new one developed from it. Lemmon and Paschal,[1] who first described the method, found it difficult to maintain a good puncture with the patient lying on his back. The divided mattress and the malleable needle overcame this trouble. The malleable needle may in the long run prove the best safeguard against breakage of the spinal needle, an accident sufficiently serious to make the use of a hard steel needle a real danger. Reports so far indicate that spinal anæsthesia maintained over several hours does not produce any detectable damage to the central nervous system; but the use of 5% procaine in glucose may be compared (not without apprehension) with the 0·5–1% used for nerve blocking elsewhere. Fraser [2] obtained satisfactory results with 1% procaine, and it should be borne in mind that lesions of the cauda equina have followed the use of strong procaine solutions.[3] Except perhaps in the hands of experts, the use of this technique for operations like appendicectomy, herniotomy and colostomy, seems unjustified, for the chance of anæsthesia wearing off before the operation is finished

3. Murray, R. O., *J.R. Army med. Cps*, June, 1943, p. 291.
4. *Guy's Hosp. Gaz.* July 10, 1943, p. 147.

1. Lemmon, W. T. and Paschal, G. W. jun. *Ann. Surg.* 1940, **111**, 141.
2. Fraser, R. J. *Anæsth. & Analges.* 1943, **22**, 38.
3. Ferguson, F. R. and Watkins, K. H. *Brit. J. Surg.* 1937–38, **25**, 735.

hardly offsets the greater difficulty of the continuous method. Whether the weight of procaine to be given for spinal anæsthesia has any close relationship to the total weight of the patient is still undecided, and it would be easy to give an overdose to an obese patient if the body-weight was taken as the sole criterion in assessing the amount. Enough is known about the action of analgesic drugs on nerve tissue to suggest that the dose of analgesic drug should be graded according to the number of nerve segments to be rendered analgesic.[4]

VERIFICATION TEST FOR SYPHILIS

In laboratories where large numbers of serological tests for syphilis are being carried out there is always a small proportion of sera in which a doubtful positive is obtained. Beveridge [5] describes a supplementary procedure for classifying these results as definitely syphilitic or non-syphilitic, known as the Kahn verification test. In 1940 Kahn pointed out that there are two types of positive reaction, the first directly associated with the immunological reaction to syphilis, and the second related to biological changes which may occur in the absence of syphilis. The positive reacting sera of normal animals belong to the second group. These two types of reaction are not differentiated by the standard serological tests, but if the Kahn test is carried out at different temperatures well-marked differences appear. The sera of syphilitic patients show a much stronger reaction at 37° C. than at 1° C. whereas the reverse is seen with non-syphilitic positive reactors. For verification purposes the standard Kahn test is done in duplicate. In one test all the tubes, pipettes, reagents, &c. are heated to 37° C.; in the other they are cooled in an ice-water bath at 2° C. The sensitivity of the Kahn test is greatly increased when performed at 37° C., and sera which are doubtful or weakly positive by the ordinary tests give clear-cut results, while the false "biological" positives may fail to appear at this temperature but are accentuated at 2° C. Some sera of syphilitic patients which are negative by the normal test show precipitation at 37° C. but none at 2° C. True sero-negative sera of non-syphilitic patients show no precipitation at 37° C. and 2° C., or some precipitation at 2° C. only. The Kahn verification test should be useful where normal serological tests are doubtful, or where the patient's clinical condition does not justify a diagnosis of syphilis. It has the merit of being easy to carry out.

THE LYMPHATICS

It has been said that progress in experimental medicine will only follow the development and mastery of new techniques. The truth of this is well illustrated by the work of the Harvard school of physiologists on the function of the lymphatic system. In his Lane lectures Drinker [6] has presented his experimental findings in their historical context, and drawn some practical lessons from his results. The function of the lymphatics—the lymph-nodes are not considered—can only be understood when studied in relation to the behaviour of the blood-capillary circulation. Together these two systems control what Claude Bernard called the *milieu interieur* of the body. From relatively simple beginnings in the fish both systems become highly complex in mammals, where they must be ready to meet a wide range of demands made on them by the different tissues. Data obtained by considerable experimental dexterity and the application of microscopical and microchemical methods allow the following conclusions to be drawn with regard to the circulatory exchanges controlling the nutrition of the tissues. There is a constant escape of water and crystalloids with a small quantity of blood protein from the normal resting blood capillaries. Activity or injury brings about a greatly increased capillary circulation in the tissues, and results in a greater loss of fluid and protein from the vessels. Were the escaping protein allowed to accumulate in the tissues its osmotic effect would prevent fluid re-entering the capillaries, and the tissues would become waterlogged. The protein, unable to pass back into the blood capillaries, readily finds its way into the lymphatics, and, where the part is moving, it is rapidly carried away in the lymph stream back into the blood. In a patient lying in bed for weeks on end, it is obvious that there will be no lymph circulation from many parts of the body. One would expect, therefore, that the protein would accumulate and the tissues rapidly become waterlogged. The fact that in many cases this does not happen is explained by a suggestion that the escaping protein is metabolised in situ by the tissues.

It was Hunter who first described the lymphatics as the great collecting system of the body, and they can undoubtedly take up particles of considerable size from the tissues. The walls of the lymph capillaries, though thin, are continuous, and firmly anchored to the surrounding tissues. The entry of particles into their lumen is probably the result of the minor stresses and strains resulting from movement. A similar mechanism probably explains the fact that red blood corpuscles may leave normal blood capillaries in small numbers while the bulk of the blood proteins are held back. Originally the lymph flow, with the exception of that from the thoracic duct, could only be studied as it left limbs that were continually massaged or kept constantly moving. Cannulation of the lymphatics from the heart and from the lungs has provided a constant stream of lymph from normally functioning organs. Among other things, such experiments have shown how extremely sensitive are the blood capillaries to anoxæmia. Thus the reduction of the oxygen saturation of the blood to 50% for a very short time leads to serious and irreversible changes in the capillary walls. It is important to remember this when the need for oxygen therapy arises. Oxygen should be given at the earliest opportunity; otherwise there will be a continuous extravasation of fluid into the tissues of the alveoli which will prevent further absorption of oxygen regardless of its concentration in the alveolar air. The lymph vessels of the skin are more capacious than the blood capillaries and they anastomose widely. There is little need for an active circulation to dispose of the small quantity of fluid escaping into resting tissues. Acute inflammation results in an excessive production of tissue fluid, and if the process develops rapidly it may give rise to a spontaneous flow of lymph. This flow by itself never suffices to remove all the escaping fluid, and so œdema results. To encourage lymph flow in order to reduce the œdema after acute inflammation is inviting danger. Where the inflammation has a bacterial origin, the organisms will be carried away in the lymph to reach the general circulation. Drinker believes that if this accumulation of fluid with a high protein content is allowed to persist round injured tissues an excessive growth of fibroblasts will take place, and subsequent scarring will be denser. The aim in treating a wound is therefore to prevent the fluid accumulating rather than to hasten its removal via the lymphatics. Drinker mentions the complete excision of all dead tissue to prevent further irritation of the surviving tissues, and complete rest to reduce the demands of the tissues for blood to a minimum. To this advice the surgeon would add the provision of external drainage, which seems to play its most important part during the first 48 hours in the case of an uncomplicated wound or burn. When adequate drainage has been provided it is permissible to apply uniform firm pressure to prevent swelling of the tissues. Turning to another

4. Clark, A. J. Mode of Action of Drugs on Cells. London, 1933.
5. Beveridge, W. J. M. *Edinb. med. J.* June, 1943, p. 344.
6. Drinker, C. K. Lane Medical Lectures: The Lymphatic System; Its part in Regulating Composition and Volume of Tissue Fluid. London: Humphrey Milford, Oxford University Press, pp. 101, 14s.

field Drinker also offers an explanation of the changes found in pulmonary silicosis. The fibrosis in the lungs develops as a result of chronic lymph stagnation and the accumulation of protein-rich fluid. This is brought about by the fibrotic stricture of the lymphatic vessels round the silica particles carried to them from the pulmonary alveoli.

There remain a number of unsolved problems in this field. For instance, why does the flow of lymph from the same organ vary widely from one animal to another of the same species? The quantities of lymph obtained bear no relation to the weight of the animal, but may conceivably reflect some difference in its nutritional state. The function of the intestinal lymphatics is not clear. It has yet to be shown experimentally what proportion of the fat ingested by a mammal leaves the gut by way of the lacteals. At the same time the thoracic duct provides a bypass enabling certain products of digestion to reach the blood without first having to pass through the liver. The answer to these and similar questions is most likely to come from the application of the careful experimental methods well illustrated by the work of Drinker and his colleagues.

PROFESSIONAL FREEDOM AND THE LCC

LAST week opened well for lovers of liberty; and on Tuesday the London County Council carried on the good work. The first of two significant decisions affecting its medical staff concerns the censorship of scientific books or articles by administrative superiors. Doctors employed by the LCC have been perfectly free to publish books and papers so long as they did not refer to their connexion with the council; but if they wanted to mention their appointment they were obliged to show their draft to the head of their department so that he could satisfy himself "that no question of policy likely to implicate the Council is involved." In its report presented on Tuesday the general purposes committee suggested that officers should be encouraged to write on their own technical or scientific subjects, and that it can safely be left to their discretion not to publish any book or article in their official capacity which will seriously implicate or embarrass the Council in regard to its policy. Accepting this view, the LCC has decided that, in writing on purely technical or scientific subjects, medical and other officers may state their LCC appointment without asking leave of their departmental chief. This enlightened ruling is, we suspect, not altogether unrelated to the call for "scientific freedom" raised by Dr. Geoffrey Bourne and others in the *British Medical Journal* during the past few months; and the second decision reached at the same meeting also betokens a welcome sensitiveness to medical public opinion. An experiment, it was agreed, is now to be made at St. James' Hospital, Balham, by which the medical superintendent will devote himself entirely to administration, and the complete clinical charge of patients will be divided between the heads of the medical, surgical, and obstetrical departments. This is another step towards liquidating the hierarchical system which has been one of the major flies in the ointment of municipal service.

ARTIFICIAL INSEMINATION

THE House of Lords, as reported on page 176, has been debating artificial insemination. In the USSR and USA especially, this practice is now widely employed by stockbreeders, who benefit greatly by a method which allows one bull to sire as many as 1000 calves in a breeding season. The rapid development of artificial insemination of animals is no doubt responsible for the new interest in its application to human beings, either as a eugenic measure or as a means of relieving the unhappiness of involuntary sterility. In the United States its use for this last purpose has evidently been making headway. A survey sponsored by the National Research Foundation for Eugenic Alleviation of Sterility provided particulars of 9489 women who had achieved at least one pregnancy by artificial insemination, and in 3649 of these the semen came from a donor other than the husband.[1] More than 97% of these pregnancies are said to have yielded normal babies.

Guttmacher[2] classifies the indications in three main groups. In the first of these, intravaginal coitus between husband and wife is impossible because of mechanical factors, among which he includes impotence, hypospadias, vaginismus, and excessive obesity. Probably all doctors will agree with John Hunter that in such circumstances artificial insemination is right and proper. There is neither moral nor legal objection; the child will no doubt be accepted at law as the true offspring and heir of the parents concerned. Guttmacher's second group comprises a miscellaneous collection of conditions including (in the woman) genital hypoplasia, cervical stenosis, uterine malpositions, and (in the man) subnormal semen. In such cases the indications are, to say the least, less definite; for these conditions are mostly amenable to treatment and should be treated accordingly. The third group—the controversial one—is that in which semen has to be provided from an outside donor, either because the husband is sterile or because he carries hereditable characters that make it inadvisable for him to beget children. The husband who discovers that he must not or cannot have a child of his own may share his wife's wish that she should be enabled to bear healthy offspring.

There is, as we have said, no legal or moral problem when the husband provides the semen; but both lawyers and moralists are profoundly concerned when insemination is performed out of wedlock. As the law stands, the child conceived in this way is a child of uncertain parentage; and Guttmacher, writing for Americans, recommends that, to avoid litigation later, it should always be adopted by its mother and nominal father.

Sir BECKWITH WHITEHOUSE, professor of midwifery and diseases of women in the University of Birmingham, died suddenly in London on July 28. He had just been nominated president of the British Medical Association for a second year. He was in his 61st year.

We also regret to announce the death on July 27 of Dr. JOHN GILMOUR, for many years senior regional medical officer to the Scottish Department of Health.

1. Seymour, F. I. and Koerner, A. *Ibid*, 1941, **116**, 2747.
2. Guttmacher, A. F. *J. Amer. med. Ass.* 1942, **120**, 442.

PORTABLE X-RAY UNITS.—In response to an appeal by Mr. Derek McCulloch for £1500 to provide a mobile X-ray unit listeners to the Children's Hour have contributed ten times this amount and £300 has been spent on a mobile X-ray unit which was presented on their behalf to Sir Ernest Clarke, chairman of the home service ambulance committee of the Joint Red Cross. The unit, which has been constructed under the direction of Mr. H. T. Ferrier, FSR, carries a team of three—senior radiographer, dark-room assistant, and driver-mechanic—and is self-contained with its own generating equipment, a high-power X-ray unit, spare X-ray tubes, and a dark room. It can be adapted for different kinds of work. In its simplest form a single transformer tank, easily carried by two men, can be set up at the patient's bedside with the control table to produce 125 mA at the usual kV values for rapid bedside chest work. For routine chest work at a clinic two small valve tanks, each handled by one man, can be joined up as a four-valve set producing 250–300 mA. The exposure of $\frac{1}{25}$–$\frac{1}{50}$ sec. at the usual teleradiographic distances is the fastest yet obtainable under mobile conditions. The control table and the other parts of the apparatus may be switched and connected to allow mass miniature radiography. Camera and identification system are automatic. A system of lagging, reverse action fans and thermostat keep the inside of the car and the processing units at an even temperature. Eleven portable X-ray units are also being supplied to children's hospitals in this country and £6000 has been sent to buy X-ray equipment for the benefit of children in Russia.

Special Articles

CHOLERA IN HONG-KONG

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DISTRICT MEDICAL OFFICER, CYPRUS; LATELY MEDICAL OFFICER, COLONIAL MEDICAL SERVICE, HONG-KONG

CHOLERA appeared in Hong-Kong in 1937 after an absence of some years. The outbreak was a severe one, and out of a total of 1690 cases there were 1082 deaths. I saw only the tail-end of this epidemic, during which hypertonic saline was, so I understand, used as routine treatment. From 1937 on, the disease remained endemic in the colony, presumably owing to the creation of carriers, for by 1940 a carrier rate of 20% was found among certain sections of the community just before the annual outbreak. The figures for the three years 1938, 1939 and 1940 show how it pays to be prepared for cholera, and are striking testimony to the efficacy of the control measures employed:

	1938	*1939*	*1940*
Cases	547	708	647
Deaths	363	448	331

In 1938 the disease was first notified on May 25. It occurred sporadically throughout June, reached epidemic proportions in July and waned as the hot season drew to its close in September. The virulence of the disease abated considerably as the summer wore on, and the case-fatality, which had been 71% in June and July, was reduced to 30–40% during August, September and October. This reduction was due in part to the rigorous imposition of a routine line of treatment for all cases. But it was mostly due to the decrease of virulence which occurs when an epidemic of any major disease is declining. The point was put neatly by one of my colleagues with Indian experience of the disease: "It doesn't matter what you do in the first three months, 70% of them will die; and in the last three months, if you feed them on Worcester Sauce, 70% of them will recover." The fatality for the 547 cases in 1938 was 55%. Many more men than women were attacked by the disease, but the fatality in the two sexes does not differ significantly. The fatality peaks are attained at the extremes of life.

CLINICAL FEATURES

The onset in cholera is usually sudden, the loss of fluid by the bowel and by mouth is exceedingly rapid, and the victims of the disease reached hospital as a rule at the end of the evacuation stage or the beginning of the stage of collapse. In these collapsed patients, the cheeks were hollow, the eyes sunken, the lips were often a little cyanosed, the fingers and toes were frequently shrivelled, the skin was inelastic, the tongue dry and centrally furred, the extremities cold, the nails blue. Their voices as a rule were reduced to a whisper—the vox choleraica—and they were not restless. Mentation was almost invariably clear, and provided cramps had not yet begun a history was usually obtainable. The important points in the history were when the disease had begun, when urine had last been passed, how many times the patient had vomited, and how many stools he had passed since onset. All patients were also asked whether they had been inoculated against cholera and whether they smoked or ate opium. The prognosis is impaired by opium addiction.

Treatment.—On admission the routine treatment adopted was as follows.* The axillary and rectal temperatures were taken and charted, rectal swabs were taken for a bacteriological examination, 1/100 gr. of atropine was given hypodermically, the blood-pressure was taken when possible, and intravenous saline infusions were begun at once. The temperature of the infused saline was regulated by the difference between skin and rectal temperatures—the greater the difference the lower the temperature of the saline—and the rate of flow was gauged by the degree of dehydration present. The saline solutions used were normal saline, bicarbonate saline (gr. 160 to the pint), and 2% glucose saline. Kaolin in suspension and potassium permanganate in pill-form, gr. 3 four-hourly, were given by mouth as routine measures throughout the epidemic. Charts were also printed to enable the amount of urine passed and the number of stools and vomits to be recorded. The importance of charting hour by hour and day by day the amount of urine passed in the reactionary stage of cholera cannot be over-emphasised. It is essential to have these urinary data kept up to the minute if a threatening anuria is to be successfully combated.

Anuria.—The two greatest dangers to life in cholera are hyperpyrexia during the reaction stage, especially after saline infusions, and anuria. The half-hourly charting of the rectal temperature during the infusion of saline and the application of ice-packs or rectal injection of iced saline were the measures employed to overcome threatening hyperpyrexia. Anuria, and its consequent uræmia, is unfortunately a common complication of the disease; the factors which cause it are the fall in systolic blood-pressure, the diminution in the minute-volume of the kidney owing to the increasing blood viscosity, and the hitherto unexplained fact that the kidney in salt-deficient animals does not secrete urine freely. One interesting clinical point is that stocky, broad-shouldered young men are more prone to develop this complication than other physical types. The earliest signs of the onset of this condition are congestion of mucous membranes and conjunctivæ, malar flush, rambling speech, delirium, and a gradual increase in depth and rate of respiration. The condition, unless promptly treated, leads invariably to coma and death. It affords a clear example of a non-gaseous type of acidosis brought about by the retention of acid radicles which results from the depression of kidney function. The only measures which appear to be rational in attempting to overcome this anuria are the six-hourly infusion of 1000–1200 c.cm. of bicarbonate saline, the giving of hot rectal salines and cupping of the loins. I have seen a man remain completely anuric for over 50 hours and yet recover completely. During the anuric phase the blood-urea rises rapidly and may reach very high figures. The man referred to above had a blood-urea of 350 mg. per 100 c.cm. at the end of his anuric period. Recovery is heralded by the passage of a few ounces of turbid, high-coloured uriñe, and this is rapidly followed by a "critical diuresis" resembling that seen in some cases of acute glomerulonephritis.

To sum up, the points on which most stress must be laid in the treatment of cholera are these: the fluid loss must be made good as rapidly as possible, and at the same time the toxæmia must be diminished by all available means. If this fluid loss is not quickly made good, the suppression of urine which invariably occurs in the stage of collapse may readily develop into an anuria leading to rapid death. Suppression occurs when the systolic blood-pressure drops below 70 mm. Hg, and it is therefore one of the aims of treatment to raise and to keep the systolic blood-pressure above that level. But if the restoration of the body fluids is brought about too rapidly the results are apt to be equally fatal, for this reason. Saline solution is being poured into the veins of a profoundly dehydrated and collapsed human being whose blood viscosity is about 1064–1070; his extremities are blue and cold; his rectal temperature may be anything up to 104° F. The circulation in the walls of his intestine has been in abeyance, if not absolutely, at any rate relatively, for many hours. The blood viscosity is rapidly reduced towards the normal figure by the infusion, the circulation is restored, and the immediate result is the absorption of a possibly lethal dose of toxin from the small intestine. That this is the course of events is shown by a study of the half-hourly rectal temperature charts taken during intravenous infusions. The rise of temperature is frequently sudden, and should it transgress 106° F. death will inevitably ensue. Controlling measures must be always at hand to prevent this disaster, and ice is much more useful in a cholera hospital than hot-water bottles. Truly did the early Anglo-Indian writers on this disease say that the reactionary stage was even more dangerous than that of collapse.

* An investigation into the treatment of cholera with sulphaguanidine was planned as soon as supplies of the drug became available. It is too early yet to say whether the drug has any bacteriostatic action on cholera vibrios. By September, 1941, only a comparatively small number of cases of cholera had been treated with the drug and the results did not appear to be significantly better than those in a control group of equal size treated with salines. The investigation was interrupted before any definite opinion had been come to about this drug and cholera.

Rogers quotes Calcutta figures to show that over a certain period no recovery was recorded in Europeans whose temperatures rose above 103° F. in the stage of reaction. This statement is happily not true for Hong-Kong if one considers the rectal and not the skin temperature. There were five European cases of cholera in 1938; one died of anuria and right-sided cardiac failure, whereas the other four recovered, one after a stormy illness in which his rectal temperature rose to over 104° F. on several occasions.

Normal saline was chosen as the routine infusion, first, because hypertonic saline had not been conspicuously successful in 1937, judging by its mortality; second, because it seemed that theoretically the main effect of hypertonic saline intravenously would be to induce a flow of fluid into the blood-stream and the only place in a choleraic body which could yield extra fluid would be the gut. This would mean that even more toxin would be absorbed and the subsequent reaction would be a violent one. To reduce this to a minimum, normal saline was chosen. Ride,[1] in a penetrating and masterly survey of some of the biochemical aspects of acute cholera, arrived at a similar conclusion, and I cannot do better than quote his words: "Until we have ascertained the chemical nature of the fluid loss it would be better and more scientific to attempt to make good the dehydration loss by normal saline infusions; until we are certain what will do the most good it would be better to use that which we know will produce the least harm, and that undoubtedly is normal saline." Ride also stresses the paramount importance of early restoration of renal circulation and function; his paper must be read in its entirety by those interested in the biochemistry of this disease.

Cholera sicca, the rarest type of the disease, was only seen three times in 1938. Two of the patients were children, the third was a young man. All three were desperately ill on admission. Cyanosis, hyperpyrexia and collapse were the outstanding signs, and one of the children, who had no diarrhœa, showed signs of free fluid in the peritoneum and shrivelled finger-tips on admission. Her temperature was 106° F. and this had to be reduced by the continuous application to the body of sheets wrung out of iced water. All these patients died, and vibrios were isolated from the intestinal contents at autopsy. Presumably in such cases the outpouring of rice-water fluid into the gut is so rapid that a paralytic ileus ensues, which accounts for the complete absence of diarrhœa.

Complications noted in this series, apart from the anuria, were septic parotitis in five cases, keratitis, boils, cellulitis, cholecystitis and various types of skin sepsis. Pulmonary conditions such as bronchitis and bronchopneumonia were not uncommon, but frank renal lesions were scarcely ever found. Many sections of kidneys taken from patients who had died anuric showed no gross microscopic changes—that is to say, the renal condition is one of functional depression rather than of structural change. One man developed and died of a right-sided pyonephrosis during convalescence, and another contracted fatal diphtheria after an attack of cholera. An interesting but unusual sequela of the disease is bradycardia. Several patients had a pulse-rate in the forties during their convalescence.

Differential diagnosis presents few difficulties in most cases, and sheer fright accounts for most of the mistaken diagnoses which were usually bacillary dysentery, gastroenteritis or food-poisoning. The two most interesting mistakes were a ruptured ectopic gestation and meningococcal meningitis with the rare so-called choleraic onset. In this condition the stools retain their fæcal pigmentation and in no way resemble the rice-water stools of true cholera. Two cases were seen in which bacillary dysentery and cholera coexisted.

Bacteriological examinations were made in 500 of this group of 547 patients. Rectal swabs were taken on admission and again during convalescence, and no patient was discharged until he had had two consecutive negative reports at an interval of a week. Vibrios persisted for remarkably long periods in some cases and this persistence was more commonly noted in children than in adults. One adult German took 31 days to become vibrio-free. The returns showed that 349 of these patients were vibrio positive, 151 vibrio negative. Some vibrio-positive cases were only found to be so on a second or third examination. Therefore 7% of all cases sent in as cholera proved to be so, while 30% were never proved to be suffering from the disease. There is little doubt that most of the 30% vibrio-negative group were really suffering from cholera, as nearly half of them died. The figures are given in the table.

Deaths				Recoveries			
Vibrio- neg.		Vibrio- pos.		Vibrio- neg.		Vibrio- pos.	
M. 46	F. 26	M. 145	F. 66	M. 57	F. 22	M. 80	F. 58
Total 72		211		79		138	

M. = male; F. = female.

MEASURES OF CONTROL

In a group of 106 patients who stated definitely that they had not been inoculated, 39 died and 67 recovered—a fatality of 38%. In a group of 26 patients who said they had been inoculated in 1938, 3 died, giving a fatality of 12%. These small-group figures prove nothing. The lower-class Chinese, who suffer more than any other class from cholera, did not come forward readily to be inoculated against cholera, and they are extraordinarily shrewd judges of the value to be attached to the various prophylactic methods now employed in medicine.

The measures necessary to combat an outbreak of cholera include rigorous supervision of immigrants, however they arrive, by land, sea or air, immediate segregation and prompt notification of all obvious or suspicious cases, and tracing each case or cluster of cases to its source. By these means it is often possible to trace and eliminate early foci of infection, such as an isolated infected well. Measures controlling the sale of fruit, food, drinks and ice-cream in the streets become essential if the disease shows signs of spreading, and sensible propaganda can be of immense value in lessening the extent of an epidemic. The five points to be stressed in propaganda are:—

1. Boil all drinking water.
2. Eat no uncooked food.
3. Be inoculated against cholera.
4. Avoid purgatives of any sort.
5. Do what you can to lessen the fly nuisance.

For the treatment of the established disease it is desirable to have a fly-proofed building with stone floors which can be swabbed at intervals through the day. The various salines should be made up in bulk, and the few instruments necessary for tying in a cannula are kept sterilised and ready for use at a moment's notice. The most convenient and accessible vein is the internal saphenous just above the internal malleolus. All dejecta should be subjected for at least an hour to 10% 'Izal' or some similar antiseptic before being disposed of, and care should be taken in planning the lay-out of a cholera hospital to see that mortuaries are as carefully fly-proofed as wards.

1. Ride, L. T. *Caduceus*, 1938.

NATIONAL ASSOCIATION FOR THE PREVENTION OF TUBERCULOSIS

MASS RADIOGRAPHY

THE association's annual conference was held in London on July 28, with the Duchess of PORTLAND in the chair. Wing-Commander R. R. TRAIL pointed out that early diagnosis is of little value unless followed by efficient treatment; it is the aim of the new allowances to facilitate such treatment. Tuberculosis is the main cause of death in the age-group 15–24; treatment of early cases would not only minimise this mortality but in the long run would save the country money.—Surgeon-Commander W. G. C. FITZPATRICK described the pioneer work of the Royal Navy with mass radiography, and mentioned the monotonous and tiring nature of the work.—Dr. P. D'ARCY HART brought out the differences between military and civilian surveys: among civilians examination is voluntary, and a higher incidence of positive findings is to be expected because Service personnel have been selected. Patients already known to be tuberculous should be included in such surveys, but they should have special consideration and

there must be no possibility of the findings leading to victimisation. About 0·5% of those examined in a civilian survey would have to leave work for diagnosis and treatment, while 1–2% would need to be kept under observation, though able to remain at work. The difficulties to be overcome are financial (partly covered by the present scheme); the deficiency of sanatorium beds; the decision as to the best treatment of certain early cases; and the rehabilitation of sputum-positive cases.—Miss K. C. CLARKE, of Ilford Ltd., thought that quality is more important than portability in miniature radiography apparatus; the sets now being supplied can be moved quickly by three men. She did not agree that the work is monotonous; the personnel can exchange duties frequently.—Dr. F. R. G. HEAF urged that full facilities for other methods of diagnosis (tomography, bronchoscopy and laboratory services) should be available before mass miniature radiography is started. Delay in diagnosis, after detection of an abnormality, may lead to invalidism. Change in environment, possibly by the introduction of prophylactic workshops and night sanatoriums, might diminish the need for treatment beds. Infected people should be regraded as workers, not invalids.

A different use for the mass-radiography sets was suggested by Dr. C. H. C. TOUSSAINT. Half the deaths from pulmonary tuberculosis occur within a year of notification; these are acute cases of rapid onset. One X-ray examination will be of little use in detecting such cases, so that the present scheme is inadequate. A better scheme would be to secure the coöperation of general practitioners, by offering free X-ray examination for any of their patients in whom a suspicion of chest disease has arisen. By adopting this idea the tuberculosis officers of Bermondsey and Southwark had detected 2·8% of active cases among those X rayed. This work had been done with full-size films, but this would be the best use for the new miniature sets.—Dr. E. K. PRITCHARD, tuberculosis officer for Southwark, supported Dr. Toussaint's views. People who suspect they are tuberculous may not present themselves for radiography, but those who have symptoms will readily come for X-ray examination if advised by their family doctor.—Some of the later speakers discussed the reactions of workpeople when a survey is proposed in their factories. An important point is that when a confirmatory examination on full-size film is required this should be arranged for in confidence.—Major PETER KERLEY maintained that the opposition to mass radiography is based on exaggeration of its difficulties. In the control of tuberculosis lack of sanatorium accommodation is the real problem. He did not agree that most cases are acute with rapid onset; cases found to have positive sputum often have no symptoms.—Dr. HARLEY WILLIAMS spoke of the necessity for intelligent propaganda as a preliminary to mass radiographic surveys.

ALLOWANCES

In opening the discussion on the new financial allowances for the tuberculous Mr. ERNEST BROWN, Minister of Health, said that the deaths from tuberculosis in the third year of this war have been less than half those in 1918, but we must not forget that the mortality from tuberculosis is an index of past rather than present conditions. There have been two obstacles to early treatment—failure to discover the disease early, and the patient's unwillingness to undergo treatment if this means his giving up work. The scheme of allowances, which ensures that patients can afford to give up work, involves an entirely new principle, for in effect it supplies benefits for the patient's dependants. It is essentially a public-health measure, and not a kind of glorified public assistance. A flat-rate, rather than a means test, has been adopted, and it is hoped to meet the inevitable anomalies with discretionary allowances over and above the maintenance scale. The allowances and the facilities for mass radiography are estimated to cost the Exchequer £3,000,000 a year when they are in full swing. Allowances are to be restricted to pulmonary cases because these are likely to respond to early treatment while earning capacity is but little impaired, and because these patients may continue at work and infect others. Neither of these considerations applies to non-pulmonary tuberculosis.

Dr. J. B. MCDOUGALL maintained that chronic cases ought to receive the allowances, if only to protect the general public from infection. It is difficult for tuberculosis officers to decide whether a case is chronic and therefore ineligible.—Mr. J. L. SMYTH, secretary of the social insurance department of the TUC, pointed out that the allowances only provide minimum subsistence for patients compelled to give up work, and are not high enough to act as an inducement to those who need early treatment but still feel well.—Dr. G. S. JOHNSTON and others agreed that difficulties will arise from the exclusion of chronic and non-pulmonary cases, and that the allowances are too low.—Mr. T. LINDSAY, principal assistant secretary to the Ministry of Health, explained that the allowances are restricted in amount, and not given to chronic or non-pulmonary cases, because they have been introduced under emergency powers. These powers permit money to be spent only on services connected with the war—for example, to promote recovery of working capacity. A more extensive scheme would require special legislation leading to delay. Relief for the chronic case unlikely to regain his working capacity would not be a war service. Extension of allowances to chronic cases might, however, be considered on the ground that such patients are a source of infection.

In England Now

A Running Commentary by Peripatetic Correspondents

I AM frankly puzzled about this social biology scheme for tackling the problem of promiscuity, and its corollary of venereal disease, in war-time. Its promoters seem to think that it is only necessary for a "training-scheme" to be offered to the young women haunting the streets and flats and dock sides for them to abandon their gay life and huge money takings and become reformed characters. Committees working for the British Social Hygiene Council propose that women who need definite medical and psychiatric treatment before they are capable of adjustment to industrial life should be directed to special training centres, with hostels attached, attended by physicians and psychiatrists from regional EMS hospitals. This scheme would apparently combine a group of women who have failed in industry because they need psychiatric treatment with a group who cannot be employed because they are deliberately promiscuous. To say that "biological causes" are involved in both cases means to me nothing at all. Who are these promiscuous women? Some are impudent hussies who have declared themselves as "prostitutes" on registration; others have been called up but have behaved so outrageously that neither the Services nor factories can tolerate them.

I do not see what this scheme has to offer that has not been tried already. What "therapeutic occupation" can be offered to console a young woman who has been dragged away from earning £30 a week in the Charing Cross Road I cannot think. It is not clear how "skilled diagnosis" is going to help, for no evidence is given to support the belief that many of them are in some way subnormal or abnormal. Nor are the Government departments concerned sympathetic. The Ministry of Labour regard the prostitutes and psychoneurotic misfits as so few that industrially they are not worth bothering about. Ministry officials have no power to control conduct or insist on treatment, no expert staffs to run experimental centres. The Ministry of Health also say they have no powers, although no doubt they would be glad to see idle women gathered off the streets and night-clubs. But the opprobrium over 33b does not encourage them to ask for further compulsory powers on health grounds. The Home Office and the police say they can do nothing within their existing powers. I think myself they could do much to clean up the streets, but not while they are uncertain whether they have public opinion behind them. No constable is going to risk his career by enforcing unpopular regulations if he is to be ruined by a mistake—or even the suspicion of a mistake.

But if we really want to discourage promiscuity we cannot allow public places to be used as open markets. Young girls are encouraged to take up evil ways when they see older comrades earning big money under the

very eyes of police and public who make no sign of disapproval. The encouragement to the potential customer is equally obvious.

* * *

To make any plan for London would be a great achievement. To have provided a practical one which incorporates such stuff as dreams are made of was a greater. Mr. J. H. Forshaw and Prof. Patrick Abercrombie in their *County of London Plan* (Macmillan, pp. 188, 12*s*. 6*d*.) have also shown us how to set about carrying it out. What is Planning? Thinking ahead. To think far enough but not too far. To think as a whole and yet in bits. This new London will not arise at the stroke of the magician's wand, but by the sweat of brows, the agonies of thought, the spirit of compromise over half a century. The men that built our cathedrals thought ahead. The men that planted oaks thought ahead. And then came the time of economic returns; and the jumbled heap of murky buildings was the result and soft woods were planted that a man might see his return before he died. Now again we begin to think ahead. Mr. Forshaw and Prof. Abercrombie can never see the realisation of their plan. They must be content if they see their first period well on the way. They should die happy if they see the second one begun.

Who is a Londoner? There are those that were born and bred here. There are those that come from all the world to earn their living here and return whence they came. And there are those that come from Liverpool and other parts of the North and West to rule and govern us, to minister to our immediate needs, and to organise for our future ones. The authors of the plan, themselves in the third category, have wisely recognised this in their division into London *the Community*, London *the Machine*, and London *the Metropolis*. In the governance of London the multiplicity of function has always been a factor of difficulty. This is not diminished when we remember that we are not only the metropolis of a country but also of an Empire, and every man and woman in that Empire has a right to a say. It is a pity that the City still stays out, unless the rulers of that area have definitely decided to plan it as a relic of a bygone medievalism. Nor can we think of London only as being within the County area. We must take into account the London *Sprawl* of 1943, as indicated on the dust cover. It is fortunate that one of its authors is also adviser of plans for both these other areas—the kernel and the husk.

Where does medicine come into the plan? Into every word of it. There is the hygiene of the home and the hygiene of the place of work. There is also the hygiene of the travel to and fro. This is a matter that has hardly been touched as yet; but upon it may depend in peace the further evolution of our state, just as in war the success of an engagement will depend upon the hygiene of the march. And so as doctors we are interested in the roads and the railways and the waterway of London, not only as human beings, but also that sore feet or fatigue may not interfere with efficiency at work or enjoyment of leisure. The engineers will deal with this. What more specially concerns us? It is a law of nature that all living organisms die from accumulation of products of their own activity, unless these are removed by nature or by art. Sanitation must come first. There is no mention of sewers in this report. Maybe that is being kept for a more private communication to the council; but it is well to remember that upon the sanitary engineer depends the success of all enlarging communities. Surface refuse comes from two sites—the market and the house. Of the former the plan takes account, the latter is outside it. Ventilation comes next, and in this the plan is sound, for open spaces are a matter of ventilation and a big factor in the prevention of slums. The whole plan is based upon the urgency of space for the unit of population—that is, the individual. But it is no use providing air if persons are allowed to foul it; "further research is necessary into the question of atmospheric pollution"—aye, and powers to prevent it. With ventilation may be linked the sun and air bath, and while our planners have not forgotten this they have been all too chary of swimming pools. Instance the development of the South Bank area—one of the high spots of the plan. But County Hall alone would more than fill one in the lunch hour of a July heat wave; and within the stretch thence to Southwark Cathedral there is need for two if not for three.

The problem of hospitals they leave as "largely a matter for the council and medical authorities to decide." Not too good, for neither of them can give unbiased views. The council is the owner of the majority of hospitals. In the interest of the county we can no more refrain from moving hospitals than from moving Waterloo station south or from putting Charing Cross underground. The "medical authorities," whoever these may be, think in terms of municipal and voluntary systems. We have to think of hospitals in terms of usage by the people, and what they want is a hospital nearby for the daily needs of illness. This was not so at the beginning of the century. For ordinary illnesses people stayed at home; they went into hospital to have something done or because they were suffering from some grave or rare disease. Now we take them in to see whether we can avoid doing anything with the knife and to discover whether they may be in the early stage of some disease while it is still curable, and most people have to go to hospital whenever they must stay in bed for more than one day. Modern accommodation and domestic economy do not allow of illness being cared for in the home. Everything other than these three needs may go to special hospitals which may be "centralised" or "decentralised"; the land alongside the "B" ring-road may be suitable for them. But for the hospital serving the daily life of the community—including childbirth—there is one place and one place only, and that is near the people's homes. It must be accessible, not "by road, rail or air," but by Nature's method of foot-slogging or carried in mummy's or daddy's arms.

And so we need a hospital for each unit of the population just as much as we do a school. The unit will be larger than those chosen for schools—perhaps five, ten or twenty times as large. When it is decided how big a hospital is economic for the daily needs of the people without doing special work, we shall need an addendum to the plan. This should allot a hospital for the daily needs of the people to each unit of population. It may be fitted in either to the Social and Functional analysis (coloured plate 1) or to the Development and Zoning plan (coloured plate 12). If there is already a hospital within the area of a given unit it does not matter whether it be under municipal or independent control so long as it is efficient. If there be no hospital in this area one should be built and an old organisation moved into it or a new one formed. If there is more than one hospital in a given area the most suitable should be allotted for this purpose and the others reserved for special work or pulled down. But no plan of London can be considered complete without the establishment of such hospitals. Perhaps the survey of hospitals that is at present being carried out will give it us. If it does not we must ask Mr. Forshaw and Prof. Abercrombie to return to a task for which they have already earned the gratitude of everyone in the Empire.

* * *

Some years ago when I was on a visit to the Mayo Clinic and had whiled away an afternoon in their public health museum it occurred to me how little in medicine we make use of mass psychology, and the idea of the decoy patient came to me. Even those masters of technique, the orthopædic surgeons, with their supporting cast of registrars and assistants, have never thought of this. We could plant in the waiting-hall outside outpatients carefully selected recovering cases, or, in the case of midwifery, normal experienced multiparæ who would allay the nervous primipara's fears by an attitude of cheerfulness and calm instead of telling them the horrible Freudian stories they usually hear.

* * *

Brown rocks, blue sky, a white-rimmed violet sea,
Grey houses, slabs of pink and gold and mauve—
Flowers on ancient walls; down cobbled street
Fish-smelling folk, wind-tanned, unwoolworthed smiles—
These are the clear-cut cameos that greet
My grateful eyes in these thrice blessed isles.
(The sea always inebriates me; in the Scillies doubly so.)

Letters to the Editor

SWABBING OF CONTACTS IN DIPHTHERIA

SIR,—I share the surprise of "Pathologists" (*Lancet*, July 17, p. 87) at two statements in the memo which you published on July 3, coming as they did from an authoritative body such as the fever group of the Society of Medical Officers of Health. The policy advocated, of dispensing with routine swabbing of contacts except in special circumstances and of restricting swabbing to those showing unhealthy nasal or pharyngeal mucosa, is likely to have unfortunate results so long as there are susceptibles in the population. One would like to know what evidence there is for the statement that the child with a healthy nose and throat is not likely to harbour the KLB for more than a brief period. There is undoubtedly much difference of opinion as to what constitutes a healthy nose and throat in a child; and in consequence, if the policy of the memo is followed, there is likely to be great variation in the number of contacts swabbed by different workers.

In a large urban community, with many possible sources of infection, action taken on the results of swabbing close contacts may fail to prevent the spread of the disease; but the general recommendation to neglect swabbing of contacts ignores the results of observations made in smaller or isolated communities where the sequence of events in an outbreak can more readily be traced. We have had recent experience of three small outbreaks which bear on these points. In the first, which involved successively three neighbouring houses, there were 8 clinical cases which occurred within a week. Repeated swabbing of the household contacts (16 persons) revealed 5 carriers, all children who had been immunised. The cases and carriers were removed to hospital, where they were kept until three successive negative swabs were obtained. No further cases have been notified in this town in the succeeding eight months. Although the carriers in this outbreak showed no obvious abnormality of the upper respiratory tract, the duration of the carrier state was 22, 44, 60, 62 and 79 days. In the other two outbreaks swabbing of the household contacts was not carried out immediately after the first cases occurred. In one instance there were 6 cases, 4 fatal, and the interval between the first and the last case was 23 days; in the other household 3 cases occurred over a period of 14 days. In these two outbreaks 5 carriers were detected after the last cases were diagnosed.

In these last two outbreaks cases occurred irregularly and the interval between cases precluded direct case-to-case infection; early swabbing of household contacts would probably have detected the source of infection and removal of the infected healthy contacts, with or without prophylactic treatment of the susceptibles, would have prevented the further spread of the disease.

To neglect swabbing of the contacts of cases of diphtheria, as recommended in the memo, will undoubtedly lead to much avoidable illness and regrettable tragedies.

Cambridge. A. W. DOWNIE.

BACK TO LISTER

SIR,—Mitchell and Buttle (*Lancet*, 1942, ii, 416) have rediscovered proflavine, and incidentally Lister's antiseptic method unaware. Cheatle (*Brit. med. J.* 1900, ii, 668) tells us that Lister supplied him with a quantity of the double cyanide of zinc and mercury from which he made a paste with 1 in 20 carbolic lotion. With this he smeared his fingers and the skin around a wound and filled up the wound, still using his fingers, and he then applied the first field dressing. Of the wounds he was able to follow up all healed with a dry scab. Cheyne wrote: "For ages, those who practised surgery were constantly confronted by the various septic diseases following wounds, whether made accidentally or by the surgeon. Occasionally, some one had a glimpse of the truth [pace Mitchell and Buttle], but the wound treatment, whatever its nature was, had as its object the application of dressings and medicaments in order to make the flesh heal, as opposed to Lister's principle of leaving the wound itself alone while striving to remove all agencies which might hinder the wound from healing" (*Joseph, Baron Lister: Centenary Volume*, Edinburgh, 1927). Lister advised the use of an antiseptic at the first dressing but never afterwards, as it would then be included among the agencies that might hinder healing. By smearing the skin around the wound Cheatle began to apply the principle of antisepsis—the exclusion of secondary infection—just smearing, covering with an antiseptic dressing and drainage for twenty-four hours or so. After this, dressings would be infrequent.

In your leading article accompanying Mitchell and Buttle's paper (p. 430) you say: "The introduction of the powder directly into the wound seems to be more logical than the time-honoured method of laying on, or lightly packing in, a piece of gauze wrung out in a 1 in 1000 watery or oily solution, of which over 80% will be retained by the gauze." This is another glimpse of the truth. It is interesting that Mitchell and Buttle observed in some cases the formation of a gelatinous material under a raised scab and rightly concluded that it was coagulated serum, the pabulum for fibroblastic growth which Lister warns us against wiping away, for he also observed it under some of his antiseptically dressed cases. The flesh was doing its job undisturbed, confirming his belief in the inhibitory powers (he was the first to use the word inhibitory in this sense) of the tissues. Proflavine is said to be less toxic than acriflavine; it is to some extent toxic because soluble. Double cyanide of zinc and mercury is one of the rare insoluble double salts and is therefore not toxic. From this mixture of salts—for it is not a true double salt—Lister made his bland antiseptic dressing. Today this is not made, unfortunately, strictly according to his final directions and it has therefore been found irritating and not strongly antiseptic (Halford, A. C. F. *Aust. J. Pharm.* Dec. 20, 1929) and so has fallen into disfavour. I suggest a perusal of Lister's method of wound management—"the principle that shall guide the practice of surgery." So quod vide and vale.

Brisbane, (Lister's Birthday). A. C. F. HALFORD.

COLLAPSE UNDER PENTOTHAL SODIUM

SIR,—Dr. Hoenigsberger's article of July 3 raises the possibility that mishaps with 'Pentothal Sodium' may not be as few as the published reports suggest. Recently I had two similar cases, one of which ended fatally. These two cases, which were seen within a week of one another, were the only ones which have caused us concern in a series of many scores in which intravenous pentothal sodium has been employed for the reduction of fractures in otherwise fit members of the Forces. In my experience, such patients are more resistant to any anæsthetic than the average civilian.

The pentothal sodium solution (5%) is always prepared immediately before use and injected slowly while the patient counts at the rate of about 1 every 2 seconds. Counting usually stops—that is, consciousness is almost lost—at between 20 and 40, when 4–8 c.cm. of solution have been given. After an interval of a minute a similar amount is injected at the same rate. A clear airway is always maintained.

CASE 1.—A soldier, aged 35, was admitted with a simple fracture of the right tibia and fibula sustained a few hours previously. His general condition was good, no abnormal signs were found in the heart or lungs and he was not suffering from shock. No morphine or other general treatment was given before admission. An hour after admission, without preoperative injection, he was given 7 c.cm. of a 5% solution of pentothal sodium and stopped counting rather abruptly at 32. Respiration and pulse were normal and his colour was good. After a minute a further 7 c.cm. was slowly given and the patient's condition appeared to be in no way unusual. Five minutes after the beginning of the injection, while the fracture was being manipulated, breathing suddenly stopped. The face was pale, but there was no cyanosis. The pupils were contracted. The pulse was rapid, weak and irregular. Artificial respiration and the administration of oxygen from a Boyle's apparatus were not successful in restoring breathing. Within 3 minutes of the onset of symptoms the pulse was imperceptible, heart sounds became inaudible and the pupils dilated. Meanwhile he was given an intracardiac injection of 2 c.cm. of nikethamide, and an intramuscular injection of 2 c.cm. of 1/1000 adrenaline solution. Artificial respiration was continued for 10 minutes, but was unsuccessful.

Autopsy revealed no pathological process in any organ, and the pathologist reported death as being due to barbiturate poisoning.

CASE 2 occurred a week after case 1. A spinster, aged 64, suffering from bruising, superficial abrasions and a simple fracture of the lower end of the left ulna was admitted as an air-raid casualty. She was very shocked, but had had no loss of blood. Her general condition was treated, and during the first 24 hours she received 2 pints of glucose saline and 2 pints of plasma by the intravenous drip method. Ten days later, when her condition was satisfactory, it was proposed to manipulate the fracture. Her previous medical history was negative. She had a moderate degree of arteriosclerosis, but no abnormal signs in heart or lungs. The urine was normal. No preoperative injection was given. After the injection of 2 c.cm. of 5% solution of pentothal sodium, at a count of 8, breathing suddenly stopped and the patient was unconscious. The pulse was 120 per minute, regular and of fair volume. The pupils were contracted and the face was pale, but there was no cyanosis. After a minute of artificial respiration the breathing re-started, the pulse dropped to 90 per minute, and a good colour soon returned to the face. She was unconscious and sufficiently relaxed for the fracture to be reduced and put into plaster. She regained consciousness an hour later and her further progress was uneventful.

In neither case were there any of the recognised contra-indications to barbiturate anæsthesia, and thinking of them in retrospect I see no way in which a repetition of these incidents might be avoided.

Cardiff. W. H. HARRIS.

SEDIMENTATION IN TUBERCULOSIS

SIR,—I do not wish to belittle the value of any serial observations on patients suffering from chronic tuberculosis, but Dr. Day's article of July 24 may do more harm than good if he convinces your readers that he has found a simple guide to progress in tuberculosis. Alas, there are no short cuts to knowledge as to how the complex human organism reacts to a chronic disease process. As I wrote in the current number of the *Practitioner*:

"... an increased rate of sedimentation in pulmonary tuberculosis can be considered of clinical significance only when it is correlated with all the clinical and radiological data, and with simultaneous determinations of plasma-protein content (by an accurate chemical method), plasma viscosity, refractive index of the plasma (permitting a rough estimate of the albumin-globulin ratio) and a complete blood-count, including a Schilling or Arneth differentiation of the polymorphonuclear cells. As facilities for such a complete investigation are rarely available in sanatorium or dispensary practice, the test is of doubtful utility in this condition."

Much more accurate hæmatological and biochemical work should be carried out, as a routine, on all sanatorium patients. The value of such findings, in close correlation with the clinical and radiological findings, would be inestimable. In the absence of facilities for such work, the educated senses of a good clinician provide a better guide to progress than laboratory findings; isolated laboratory findings expressed with the authority of mathematical accuracy may even interfere with clinical judgment.

Finsbury. E. OBERMER.

CETAVLON AND SKIN INFECTIONS

SIR,—The detergent and antiseptic properties of 'Cetavlon'[1] described by Barnes,[2] suggested a trial of this chemical at an EMS hospital in two skin wards occupied by soldiers, many of whom had streptococcal or staphylococcal skin lesions.

The two wash-basins and two baths in each ward were formerly cleaned with an abrasive soap 'Bon Ami' or with 1 in 20 carbolic acid swabbed over after cleaning with soap. After cleaning in this manner it was usually possible to grow coliforms, proteus, streptococci or staphylococci in cultures from the basins. This was not surprising, for they were likely to be greasy with the ointments used on patients, and their surfaces were worn and had cracks in the glaze. A 2% cetavlon solution removed dirt and grease rapidly, and was approved by the nursing staff. Subsequent cultures showed the surfaces to be sterile, and the method appears effective for preventing cross-infection.

Cetavlon was also found useful for cleansing the skin of ointments, and for the removal of scabs and crusts from impetiginised areas or where there was widespread dermatitis or eczema. In the initial experiments two patients with generalised boils were washed down with 1% solution daily, and the skin rinsed and dried. One of them had also an area of dermatitis due to strapping. Both cleared in ten days. In such cases cetavlon readily removes dirt and grease and reduces the staphylococcal population of the skin; the natural bactericidal powers of the skin should then suffice to deal with the infection. A case with severe nummular eczema which had had two relapses (sensitisation to flavine being suspected), a severe chronic infective dermatitis, and cases of impetigo of the face were cleaned once or twice daily with cetavlon and progress was satisfactory. Absence of the trauma involved when oil or soap and water are used must be of importance in the treatment of inflamed and infected skins.

There is no doubt that some individuals show intolerance, but the work of Williams et al.[3] indicates that the proportion is small. However one of our cases of impetigo of the face developed moderately severe dermatitis after the use of cetavlon twice daily for six days to remove crusts. Two other patients, with generalised impetigo, complained of dryness of the skin, but the application of cetavlon was continued and no dermatitis attributable to its use could be detected at the end of a week.

My thanks are due to Sister G. M. Jones and the staff of the ward, to Dr. Bodoana of the LCC pathological department for carrying out the cultures, and to Imperial Chemical Industries Ltd. for supplies.

Devonshire Place, W.1. L. FORMAN.

FUTURE OF RADIOLOGICAL PRACTICE

SIR,—In view of the probability that a comprehensive medical service may be introduced by the Government it is generally felt that the time has come when further steps should be taken to safeguard the interests of medical radiologists in such a service. We therefore invite medical radiologists to a mass meeting to be held on Saturday, Aug. 7, at 11 AM, in the Reid-Knox Hall at 32, Welbeck Street, London, W.1, when all those interested in the future of radiology will have an opportunity of expressing their views.

R. E ROBERTS,
J. DUNCAN WHITE.

COAGULASE-POSITIVE STAPHYLOCOCCI

SIR,—Referring to the article on the slide-test by Cadness-Graves et al. (*Lancet*, June 12, p. 736) it is of interest to note that during a similar investigation in this laboratory the chief source of error was found to be false positive results, given by about 10% of non-pathogenic *albus* strains, which persisted with serum and seemed to be due to agglutinins. No false negative reactions with *Staph. pyogenes* were recorded. Birch-Hirschfeld has shown that this clumping phenomenon is due mainly to the prothrombin fraction of the plasma and that no clumping at all occurs with pure fibrinogen solutions. Unfortunately the preparation of a fibrinogen-free prothrombin solution is not a simple operation for a routine bacteriological laboratory, and rather robs the test of its simplicity. The substitution of plasma, however, by a prothrombin-fibrinogen solution greatly improves the specificity of the test and this simply prepared solution is, in many ways, more convenient than plasma. The reaction is remarkably sensitive, but varies with different strains, and its quantitative nature appears to be roughly parallel with the time taken to coagulate plasma. Birch-Hirschfeld has also shown that the agglutination and coagulation activity seem, to a certain degree, to be independent. Thus a high concentration of sodium chloride (above 15%) tends to inhibit agglutination but not coagulation, while coagulation does not occur with high dilutions of prothrombin-fibrinogen solution when agglutination is still obtainable. Fresh young cultures are the most reliable and those grown on blood agar appear to give stronger reactions than those of the same organism on plain agar. The reaction is not affected by the usual

1. Cetyl trimethyl ammonium bromide, Imperial Chemical Industries Ltd. Formerly called 'CTAB.'
2. Barnes, J. M. *Lancet*, 1942, i, 531.
3. Williams, R., Clayton-Cooper, B., Duncan, J. McK. and Miles, E. *Ibid*, 1943, i, 522.

anti-coagulants and the chief sources of error associated with the tube coagulase test are obviated. The test has been found to be particularly convenient and dependable in routine work, providing the precautions stressed by Cadness-Graves and his co-workers, regarding the mixing of the bacterial growth and fluid, are observed. Details of this investigation will be published elsewhere.

West Riding Public Health Laboratory, Wakefield. R. HODGSON, FIMLT

Parliament

ON THE FLOOR OF THE HOUSE

MEDICUS MP

JULY 27, 1943.—Mr. Winston Churchill announces the end of Mussolini's long and severe reign over the Italian people to a crowded and cheerful House of Commons. The date is worth noting because events move so rapidly that it is well to measure these things from a fixed datum line. The base line for the Axis, however, was July 19 when Hitler and Mussolini met at Verona and Mussolini came away empty.

These vast changes bring us nearer the relief and rehabilitation of enemy and enemy-occupied territory alike on which so much of the future of Europe depends. Mr. Harcourt Johnstone, secretary of the Overseas Trade Department, speaking of the future of our export trade, told the House that "the relief of the distressed countries must be and is being kept in mind." He added that we shall have to share what we have with our less fortunate neighbours on the Continent and that there would be some measure of restriction on home consumption and some direction of our exports would continue to be necessary in the early days of peace.

Mr. Hudson opened his review of agriculture by paying tribute to the recent conference on world food production at Hot Springs, Virginia. "One of the most striking facts which emerged from that conference was the general agreement that immediately after the war the world would be faced with an acute shortage of food." Because of this agriculture will have to remain fully mobilised for some years. There will be not only a shortage of livestock, oils and fats but also of bread grains and rice. This is the first time that a shortage of bread grains has been prophesied by a member of the Government, and it is significant of the realisation that the demand for food will come not only from Europe and Russia but also from China and other parts of the Far East. "Therefore we may say with confidence," said Mr. Hudson, "that at all events the first two years after hostilities have ceased will be years of great stringency on the food front." To meet this stringency we need to maintain our present production for the land and to get some slight increase of our tillage area, but we have got nearly all we can in that direction. What we can increase, Mr. Hudson thinks, is our livestock. We must rear more calves and increase the number of our sheep and breeding sows.

For the last two days of the week the House discussed the white paper on education, on which a bill will be based and presented to the House later this year. The plan sketched out in the white paper envisages the school-leaving age raised to 15 and later to 16 on "appointed" days to be chosen at some unspecified date. Members remembered the Education Act of 1918 with its great promises, and the Minister himself instanced that in only one locality have the powers to institute continuing legislation been used. Much of the debate turned on the compromise on the religious instruction question which threatens to become a very hotly contested issue. On the first day of debate only one member called attention to the physical aspect of education and called for a service providing school meals for every child in every school irrespective of the means of the parents. The same member called attention to a sentence in the white paper which states that when a comprehensive national health service is set up "it will no longer be necessary for local education authorities to provide treatment, and their functions will be confined to providing medical inspection . . ." To sweep away the school clinics which have long done such admirable work would be a great mistake and the President of the Board is not likely to allow it. But the wording is unfortunate. So too is the wording of the paragraph dealing with handicapped children which says merely that part V of the Education Act of 1921 which makes provision for these children "will require substantial modification." Perhaps this issue is also to be relegated to the time when Assumption B of the Beveridge report is implemented. The House is getting into a bad habit of passing the buck to the medical profession, without giving the profession the necessary tools to do the job.

FROM THE PRESS GALLERY

Making Milk Safe

IN the House of Lords on July 27 Lord ADDISON called the attention of the Government to certain aspects of food policy, with special reference to milk and milk products and their cleanliness and safety. He welcomed the Government's white-paper on milk policy as a great organised step forward. The state was going to see that this vital food not only became more popular but was also wholesome, and it was sensibly tackling the question in the right way, beginning with the cow. Lord Addison felt sure that it would not be more than a few years before the milking herds of this country would be immensely improved. But so long as there was a considerable proportion of milk which was not bacteriologically of the right standard it was for the Ministry of Food to see that it was made wholesome. The method proposed in the white-paper was "heat treatment," which meant, he supposed, pasteurisation or sterilisation. Speaking as a medical man he thought that a great deal of nonsense had been talked about damaging milk by pasteurising it. A child would benefit by having pasteurised milk rather than none at all. The Royal College of Physicians unanimously found that milk was not damaged by being pasteurised, and some time ago the BMA came to the same conclusion with, he thought, only one dissentient. If there were some trivial destruction of vitamin content, that could readily be made good.

MINISTRY'S MEDICAL ADVISER EXPLAINS

Lord HORDER was on the whole satisfied with the policy outlined in the white-paper but he reminded the Minister that time was of the essence of the contract. He welcomed the joint responsibility of the ministers of Agriculture and of Food for the distribution of clean milk—which he likened to the double security of two trustees signing a cheque. But there was one exception to the satisfaction which medical men and women felt with regard to the safeguards. He believed that much accredited milk was not obtained from tuberculin-tested cows, and if that was so, why should it not be an offence to sell such milk unpasteurised? Although the Ministry of Agriculture was taking over the supervision of the conditions of milk production Lord Horder hoped that the local authorities would still hold a watching brief for the consumer and continue to take samples, especially of milk supplied to nurseries, schools, and canteens. There should be bacteriological tests as well as tests for keeping qualities. It was an anomaly that in this year of grace 1943 this nation should purvey, the Minister of Food condoning, a basic article of food knowing it to be a germ-spreading medium and knowing that the position, owing to difficulties of distribution, was worsening rather than getting better. Lord Horder supported Lord Addison's plea that the milk position should at last be cleaned up. It was not true that the medical profession were divided; there was as complete unanimity in the profession on this point as on any question in a free country like ours where a few folk will always take pleasure in showing their freedom by differing from the great majority. There was a note of drama about tuberculosis, Lord Horder continued, which tended to lessen the significance of other diseases spread by germ-laden milk, but, taken together, their prevalence and mortality must far outweigh those due to tuberculosis. There were two ways of making milk safe. The first was to ensure that the dairy cows were free from disease and that the processes of collection and distribution were clean. The other was

to pasteurise the milk. Both ways were good, and they were not incompatible. But the long-term policy alone was not enough. It would take several decades before anything like complete cleanliness was effected at the cow end. Meanwhile more must be done to encourage intelligent men and women to enter the ranks of veterinary science. A third method of making milk safe for consumption was by boiling, but boiled milk should not be given to babies for two reasons. First, boiling lowered its nutritive value, whereas pasteurisation did not. Secondly, to warn mothers not to give milk to their babies unless it was boiled was to stigmatise milk, and thousands of women would not give it to their children at all. In face of this the Minister of Food had wisely decided to pasteurise bulked milk. True, pasteurising plants needed steel, but since we release steel in large quantities for the destruction of life it might not be a bad thing to release a little for the preservation of life. He believed the public was sufficiently educated to prefer safe milk to milk "straight from the cow." The cover offered the small producer-retailer who might be affected would, he thought, satisfy even Lord Beaverbrook. If pasteurisation led to the shutting down of some of the dirtier milk handling and distributing premises so much the better for the community. No subsidy could be better spent than in protecting the citizen from a danger that has been in our midst far too long.

Lord TEVIOT, speaking as a convinced opponent of tampering with food, saw no justification in embarking on a pasteurisation scheme without a great deal more research and asked for a drastic policy of cleaning up dairy herds, particularly bulls. Lord HANKEY paid tribute to Lord Woolton in the words of Cicero—in nothing do men more nearly approach the gods than in giving health to men—but admitted he was uneasy about accredited milk. Lord DE LA WARR pointed out that one of the main limitations in improving our milk-supply was the need for an adequate water-supply on the farms.

MINISTER'S REPLY

Lord WOOLTON said that in London 96% of the milk was already pasteurised, in Manchester 85%, and in Glasgow 70%, and in areas of over 10,000 population 65%. It was estimated that within the next few months the amount of pasteurised milk in these areas would be increased by another 15%, and in eighteen months the whole of the country would be covered by rationalisation schemes. The problem was to get new plant to deal with the increased quantity of milk. As a broad statement, the rationalisation schemes would deal with all the places where bulked milk was distributed. He did not know whether he could secure that no TT milk was bulked, but he would try to direct it to the large centres where children should have it, or where it would be purchased as TT milk. In formulating his milk policy Lord Woolton had consulted Lord Horder, the Medical Research Council, the BMA and the Royal Colleges of Physicians and Surgeons. Indeed he had taken so much advice he wondered that he had produced a white-paper at all. He assured Lord Teviot that though he did not claim that pasteurisation gave immortality, he refused to admit that it does any harm to milk. Lord Teviot's conception of dead germs floating in pasteurised milk and rising to life again in the human body was sheer scientific nonsense. Lord Woolton agreed with Lord Horder's suggestion that even within the limitations made there was a danger of tubercle from accredited herds, but if they had waited for agreement on perfection before bringing out the white-paper they would have had to wait a long time. The Minister of Agriculture and he knew only too well the mechanical hindrances to getting more milk treated during the next eighteen months owing to the demands of the war for the machinery involved. But they hoped Lord Horder would not think they had been half-hearted. He was confident that the steps laid down in the white-paper would benefit the health of the nation long after the war was over.

Workmen's Compensation

The HOME SECRETARY informed Mr. ARTHUR GREENWOOD on July 28 that the Government had had under consideration the claims put forward from various quarters for increasing the rates payable under the existing Workmen's Compensation Acts and after lengthy discussions with the Trades Union Congress and the British Employers Confederation had decided to submit to Parliament a bill embodying certain increases. The increases were intended to be of a temporary nature and were without prejudice to the introduction of a revised scheme of workmen's compensation which the Government had under consideration in connexion with the Beveridge report. Later the bill was introduced and read a first time.

Artificial Insemination

In the House of Lords on July 28 Lord BRABAZON drew attention to the immediate consequences to our livestock of applying recently gained experimental knowledge of insemination, and to the potential results for the human race. Having achieved the highest economy in running the mammalian body as a heat engine Nature in her wisdom had thought fit to ensure survival of species by mass assault—to the tune of 3000 million sperms per coitus in the stallion, where only one was needed to fertilise the ovum. We in ours could trap the surplus and insert it efficiently into other mares. By this practice a bull could put ten cows in calf instead of one; in Russia from one ram they had got over 2,700 ewes in a year. The sperms of a stallion lasted no more than twelve hours; bull's or ram's could be kept for a week. In future we might export sperms rather than animals. To avoid the dangers of in-breeding (which had already spoilt the stock of fox and Irish terriers) the Jockey Club allowed no thoroughbred to be inseminated except by the covering stallion. Passing to the human side, from "insemination" to "telegenesis" (which means the same), there had been, he said, ten thousand applications in the USA for insemination by an unknown father from wives with sterile husbands. Such progeny, looked upon by the public as legitimate, was in fact illegitimate. Then there were women who would like to have children without marrying. In face of these new forces we must direct them so as to bring happiness and good into the world.

Lord GLENTANAR insisted that little was known as yet about the ultimate results in animals of these unnatural practices.—Lord MARLEY hoped that the new approach might be the means of ridding us of the term "illegitimate" as applied to offspring.—Lord BLEDISLOE remarked that there was nothing new about the artificial insemination of livestock. In New Zealand, whose economic prosperity was bound up with the dairying industry, it had the encouragement of Government. An official report had calculated the production in one season from one outstanding bull of 600 daughters, capable of providing 150,000 lb. of butter fat valued at £10,000. He would like the supply of semen to be accelerated so as to replenish the livestock in devastated countries.—The BISHOP OF CHICHESTER drew a sharp distinction between insemination in man and other mammals, endorsing Aldous Huxley's warning of the fearful calamity of a purely mechanical world so far as human beings are concerned.—Lord SEMPILL also looked with alarm upon the advent of these scientific ideas into the realm of human reproduction.

Replying, the Duke of NORFOLK assured the House that the Ministry of Health was closely watching artificial insemination from the human side. If and when that aspect became a live issue no doubt the Lord Chancellor would be consulted on the legal problems it raised. On the animal side it was certainly no new thing; the Arabs bred their horses by it centuries ago. Today modern methods provided a means of improving livestock in a way hitherto impossible. The use of a valuable sire could thereby be extended numerically and made available to the small farmer. But so far there had been no commercial application. In 1936 the Thoroughbred Breeders Association had laid down that insemination should only take place for the benefit of the mare, not to save the sire. Obviously the method raised immense possibilities in the restocking of Europe, but time was necessary to decide whether a particular sire was good or bad; breeders must go slowly and carefully. Large-scale field trials were, however, in train at Cambridge and Reading, and regulations relating to cattle were nearly ready to lay before Parliament.

QUESTION TIME

Diseases not attributable to Service

Mr. T. E. N. DRIBERG asked the Minister of Pensions if he would circulate the list of diseases held by the current consensus of medical opinion to be neither caused nor aggravated by military service.—Sir W. WOMERSLEY replied: It is impossible to extract from all the diseases known to medical science a complete list of those in the causation or worsening of which war service would be unlikely to play any part. There are, however, certain diseases or groups of diseases the onset or development of which would normally be unaffected by service, and of which the following are common examples. It should not be assumed, however, that every case in which the disability is due to one of these diseases is necessarily rejected.

(1) Malignant diseases with certain well-recognised exceptions; (2) Certain diseases of the glands, for example, lymphadenoma; (3) Certain diseases of the nervous system of developmental origin, for example, syringomyelia; (4) Certain diseases of the blood and blood-forming organs, such as leukæmia; (5) Progressive visual changes due to errors of refraction; (6) Venereal diseases.

Army Consultants

Replying to a question, Sir JAMES GRIGG stated that the following are members of the Army Medical Department Consultants Committee:

Major-Generals.—D. C. Munro (consulting surgeon to the army), A. G. Biggam (consulting physician to the army); L. T. Poole (director of pathology); D. T. Richardson (director of hygiene); C. Max Page (consulting surgeon); A. B. Austin, LDS (director of army dental services); A. W. Stott (consulting physician).

Brigadiers.—F. D. Howitt (consultant in physical medicine to the army); A. S. Daly (consulting anæsthetist to the army); J. R. Rees (consulting psychiatrist to the army); Sir Stewart Duke-Elder (consultant in ophthalmology to the army); D. B. McGrigor (consultant in radiology to the army); George Riddoch (consulting neurologist to the army); M. L. Formby (consultant in otorhinology to the army); R. M. B. McKenna (consulting dermatologist to the army); L. E. H. Whitby (consultant in resuscitation and blood transfusion); Hugh Cairns (consulting neurosurgeon to the army); W. Rowley Bristow (consulting orthopædic surgeon to the army); Harry Stobie (consulting dental surgeon); William Anderson, H. C. Edwards, A. Hedley White, F. A. Stammers and A. E. Porritt (consulting surgeons); Dudley Buxton (consulting orthopædic surgeon); W. D. Small, R. C. Priest, and D. F. Stephenson (consulting physicians); H. A. Sandiford (director of psychiatry).

Number of Births

Replying to a question Mr. BROWN gave the following figures for England and Wales:

Date	*Total live births*	*Illegitimate live births*
1923	758,131	31,522
1933	580,413	25,408
1942	655,075	35,164

Obituary

HAROLD ERNEST GAMLEN

M B DURH, D P H

Dr. H. E. Gamlen died at North Cheriton, Somerset, on July 26, at the age of 72, after a long and trying illness which was the legacy of his pioneer work with X rays. Having qualified at Newcastle in 1893 and taken his DPH he was MOH for West Hartlepool before making the decision to specialise in radiology. He became X-ray surgeon to the Cameron and Hartlepools hospitals, practising also in Newcastle, and to this period belong his papers on the X-ray treatment of superficial cancers and of rheumatoid arthritis by high-frequency currents. During the last war he served with the BEF as major RAMC at the 11th General Hospital and as consulting radiologist to the IE Force. In 1916 he published his method for the localisation for foreign bodies. When, some twenty years ago, he was forced to retire from his work in the North he settled in Somerset. Of his later years J. B. McD. writes:

"Gamlen made valuable contributions to radiology when it was still in the earliest and most critical stage of development. That he had endangered his own life in his work worried him little. He endured suffering, submitted to operations and, in the intervals, selected to breed his beloved scotch terriers, a hobby which he pursued with the same enthusiasm and success as had characterised his medical work. A grateful country pitied him but it was left to Gamlen himself to mould his future within the limitations of his physical affliction. Few know what struggles this entailed, but he was blessed with friends—none more than his surgical colleagues who came to his rescue so often—and the constant companionship and encouragement of his wife did much to lighten his burden."

Notes and News

PRACTICAL GUIDE TO THE SULPHONAMIDES

IN eight years the therapeutic applications of the sulphonamides have widened until these drugs must be approaching aspirin and stomach powders in popularity. This rapid success has brought its own complications: and as each new compound is introduced the general practitioner must wonder whether it is indeed the great advance it is said to be, or merely an old friend under a new name. To solve some of these difficulties a booklet of 46 pages has been prepared by a group of experts and issued as the Medical Research Council War Memo No. 10 (*Medical Uses of the Sulphonamides*, HM Stationery Office, 9*d*.). The reader should not be misled by the modesty of its format, nor by its title, for it contains all the available information needed to ensure the proper use of sulphonamides in both medicine and surgery. The booklet opens with a brief description of the chemistry, pharmacology and mode of action of the compounds; it then sets out the general principles governing their administration and a scheme of dosage which will meet most requirements. The common infections are taken in turn, and there are special sections on subjects of war-time importance such as wounds, burns and gas gangrene. The possible toxic complications are described and practical measures are recommended for their avoidance. Finally an appendix contains directions for such laboratory procedures as estimation of blood concentrations and the detection of sulphonamide-resistant strains of organisms. The doctor who is working without laboratory facilities should not be put off by the frequent references to these aids to a more scientific use of the drugs. If it is possible to estimate the concentration of sulphathiazole in the blood of an acutely ill patient valuable information is often gained and treatment can be modified accordingly. But if such estimations are not possible the drugs can still be used with reasonable safety and success, provided that the rules here laid down are applied with common sense.

Royal College of Physicians of London

At a comitia held on July 29, with Lord Moran, the president, in the chair, the following fellows were elected officers for the ensuing year:

Censors: Prof. F. S. Langmead, Dr. A. G. Gibson, Dr. G. E. S. Ward and Dr. Geoffrey Marshall; treasurer: Dr. C. Hinds Howell; registrar: Dr. H. E. A. Boldero; Harveian Librarian: Dr. Arnold Chaplin; assistant registrar: Dr. Alan Moncrieff; members of the library committee: Dr. Henry MacCormac, Dr. Reginald Hilton, Dr. Cyril Elgood and Dr. Archibald Gilpin; finance committee: Dr. George Graham, Dr. Maurice Shaw and Dr. Kenneth Harris.

The Baly medal was awarded to Prof. F. C. Bartlett, FRS, for his work on the science of physiology and in particular his contributions in experimental psychology; the Gilbert Blane medal to Surgeon-Commander D. P. Gurd, RN, and the Murchison scholarship to Dr. Bruce Cruickshank. Lord Dawson was re-elected representative on the governing body of the British Postgraduate Medical School and Dr. J. H. Towers a representative on the council of King's College, University of Durham. Dr. W. E. Hume will deliver the Harveian oration on Oct. 18.

The following having satisfied the censors' board were elected to the membership:

A. O. Bech, MB CAMB., Conrad Bremer, MD LEEDS, flying-officer RAFVR, G. M. Brown, MD QUEEN'S UNIV., ONTARIO, J. W. L. Doust, MB LOND., lieutenant RAMC, L. P. R. Fourman, MB LOND., C. Raymond Greene, DM OXFD, Margaret E. Harker, MB LOND., lieutenant RAMC, R. J. Harrison, MB LOND., J. R. Hindmarsh, MD DURH., flight-lieutenant RAF, P. M. Inman, MB SHEFF., E. G. Jones, MB LOND., S. J. R. Macoun, MB CAMB., P. J. W. Mills, LRCP, R. G. Moore, MB LOND., G. O. Richardson, MD CAMB., flight-lieutenant RAFVR, R. E. Roberts, MD LPOOL, Dorothy S. Russell, MD LOND., D. S. Short, MB CAMB., Dorothy W. Smith, MB BIRM., J. C. S. Thomas, LRCP, A. S. Watts, MB LOND., Charles Wilcocks, MD MANC., and Constance A. P. Wood, LRCP, FFP.

Licences to practise were conferred upon 223 candidates (198 men and 25 women) who have passed the final examination of the conjoint board and have complied with the by-laws of the college. The following are the names of the successful candidates:

F. A. Adcock, Joseph Ainsworth, Sheila W. Anderson, J. K. Argo, L. E. Arundell, J. D. Auton, G. B. Barker, A. S. Barling, C. H. Barnett, A. E. Batchelor, D. C. Beatty, William Beautyman, Kathleen, N. Berger, G. R. T. Birtwhistle, W. A. Ll. Bowen, R. M. Boyce, J. B. Brass, D. B. Brewer, A. J. Briggs, Alexis Brook, Barbara G. Bull, J. C. Burne, M. O. Carruthers, Jack Carter, Margaret J. Cash, Keith Chitty, C. J. Christmas, H. P. Clarke, M. H. Clement, Beatrice D. Cluley, L. H. Collier, Gladys C. Collings, D. M. Colyer, Doris E. Counsell, J. G. Coxon, F. M. Cryer, J. H. Cule, K. G. Cuming, P. N. Cunliffe, Rosalind M. L. Darby, J. C. A. Davies,

T. M. Davies, Trevor Davies, William Davies, Winifred M. Davies, M. B. Devas, Gabriel de Vesselitsky Merriman, Sheila Donahue, D. C. Dougherty, M. A. C. Dowling, D. C. H. Draffin, Margaret Duncan, P. V. C. W. Dupré, B. J. M. Duxbury, E. M. Edwards, B. H. Egerton, G. S. Emtage, G. P. Enoch, F. H. Epstein, D. M. Evans, Hassam Fakim, Albert Feldman, J. A. Fewings, M. M. Figgis, M. A. Filose, O. D. Fisher, Frank Fletcher, K. W. Forber, D. Y. Foster, Wallace Fox, H. A. Fraser, A. G. Freeman, R. J. T. Gardiner, M. R. Geake, R. V. Gibson, T. J. Gilmore, Harold Goldberg, Gerald Goodall-Copestake, A. W. G. Goolden, R. H. Gorrill, R. L. A. Gouges-d'Agincourt, S. H. Gould, Benjamin Green, W. H. Greenwood, I. L. Gregory, A. P. Grimbly, H. C. Gupta, D. L. Guthrie, R. M. Harvey, D. E. Hayes, J. S. Hayward, Michael Hemming, Jack Henneman, S. P. Higham, Gavin Hildick-Smith, G. F. Hird, C. A. Hodge, Monica M. Hogben, Herbert Holden, G. M. Homan, Philip Hopkins, M. C. Hudson Bennett, G. E. Hughes, E. A. J. Imoesi, W. N. Ingham, Frank James, G. A. James, C. W. L. Jeanes, Ursula Jerram, R. E. W. Jesson, H. D. Jesudason, G. M. Jewson, A. G. Jones, B. V. Jones, L. G. G. Jones, D. A. G. Kaye, A. R. Kenderdine, S. M. Kingsley, R. F. S. Kirkham, Gershon Kohn, C. D. Laidlaw, J. W. Langley, R. W. Lawrie, W. F. Leith, Myer Leven, C. L. Lewis, E. H. Lewis, Gwenda M. Lewis, John Lister, R. H. Little, Renate M. E. Loeser, J. B. Lyon, I. M. MacArthur, M. D. McCready, N. G. McGuire, D. H. Mackenzie, R. M. MacPhail, A. K. Mant, H. L. Massiah, Colin Maxwell-Muller, J. B. Mee, J. B. Mehta, H. P. Merrick, Margaret E. Milter, L. L. Mistlin, J. B. Mitchell, A. J. Moon, Ambrose Morgan, Gwenllian B. Morgan, Ivy M. Morgans, J. S. J. Morley, J. D. Morris, F. G. Morse, M. V. Mulye, A. P. M. Nicol, Peggy K. L. Orton, B. G. Paul, A. N. Pearson, W. E. R. Pitt, Betty J. Poland, K. I. Price, K. J. Randall, B. O. Reed, J. M. Rees, M. F. Remy, B. W. Rhodes, P. G. Roads, B. V. Robinson, K. C. Robinson, Charles Romer, A. J. F. Saxton, K. H. L. Scougall, R. H. Sewell, H. M. G. Shanly, S. S. Short, B. S. Skinner, A. N. Smith, G. B. Smith, R. S. Smith, I. S. Staddon, C. S. M. Stephen, D. M. Stevens, Janet A. M. M. Stevenson, R. H. Stillman, Alexander Stone, T. J. Swaffield, P. E. Sylvester, J. L. Taylor, G. A. Terry, G. D. Thomas, Greta C. Thompson, W. G. Thomson, Cecily M. Tinker, Salo Tischler, W. H. Townsend, Willie Townsley, John Tregilius, C. E. Tudor, R. W. Tudor, G. E. E. Usher Somers, S. B. van der Merwe, E. G. Wade, M. T. Wade, Jack Waldman, M. F. C. Walker, E. L. Ward, F. A. Watkins, Roy Webb, J. O. M. Wedderburn, W. G. White, J. P. Whitehead, J. P. S. Whitehead, Marjorie Whitney, H. S. C. Wight, R. R. L. Wild, Audrey S. Willis, J. S. Winter, R. J. T. Woodland, A. J. W. Woodroffe, R. M. Woodside, Fred Wrigley, W. D. Wylie and D. E. Yates.

Diplomas in public health, psychological medicine, laryngology and otology, and anæsthetics were conferred on those named at the meetings of the Royal College of Surgeons in our issues of June 19 (p. 792) and July 17 (p. 90), and diplomas in ophthalmic medicine and surgery and medical radiology on those named below.

Royal College of Surgeons of England

At a meeting of the council held on July 29, with Sir Alfred Webb-Johnson, the president, in the chair, Sir Arthur Keith was reappointed representative on the joint committee for Anthropological Research and Training for 1943–47. It was decided to continue the recognition of the posts of RSO and first house-surgeon Kent and Sussex Hospital under the FRCS regulations, and to extend it to include the post of second house-surgeon.

Diplomas of membership were granted to the candidates named above. The following diplomas were also granted jointly with the Royal College of Physicians:

DOMS.—J. H. Austin, Hugh Bannerman, M. K. Fleischer, Alan Holmes-Smith, William Ingman, W., H. R. Jeremy, Herbert Kirchenberger, R. S. MacLatchy, W. M. Rich, D. J. N. Smith, Alan Stanworth and E. S. Tan.

DMR.—E. M. Japha, H. G. Jones, Kathleen J. Mulvany, G. B. Stanford and E. M. Ungar.

Scottish Conjoint Board

At recent examinations of the board of the Royal Colleges of Physicians and Surgeons of Edinburgh, and the Royal Faculty of Physicians and Surgeons of Glasgow the following were successful: LRCP & SE, LRFP & S

J. E. K. Butchart, J. B. Chetwynd, E. J. Connolly, P. M. Ellison, Julius Honig, Samuel Hellowell, R. H. Johnson, W. S. Joyce, W. B. Kalish, P. D. Kemp, Leonard Le Vann, Werner Levy, V. H. McGettigan, William McKenzie, Andrew Marshall, Paul Menko, T. S. Moore, H. D. Morgenbesser, C. E. Phillip, C. E. Ratner, W. M. Robinson, Olga C. Rollason, Aaron Simons, Bernard Snell, W. R. Steven, N. C. Wollin and Milton Zises.

Willi Hoffer, MD VIENNA, and Ernst Levin, MD MUNICH, graduates of recognised foreign universities, were also admitted licentiates.

Ambulances To and From London

Ambulances of the headquarters' fleet of the Order of St. John and British Red Cross Society returning empty to London from districts outside the Metropolitan area may be used to carry patients from the country to the London hospitals. Medical practitioners who have patients resident more than forty miles from London requiring transport to London should write to the joint secretaries, Home Service Ambulance Committee, 12, Grosvenor Crescent, S.W.1, two days before the date of the journey to ascertain whether the department will have an ambulance in their district in which the patient could travel.

Royal College of Obstetricians and Gynæcologists

The Council have received a gift of £1000 from a fellow to commemorate the presidency and knighthood of Sir William Fletcher Shaw. The interest from the gift will form a scholarship to be awarded triennially for research.

Infectious Disease in England and Wales

WEEK ENDED JULY 24

Notifications.—The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 2099; whooping-cough, 2081; diphtheria, 591; paratyphoid, 9; typhoid, 10; measles (excluding rubella), 2486; pneumonia (primary or influenzal), 445; puerperal pyrexia, 152; cerebrospinal fever, 44; poliomyelitis, 5; polio-encephalitis, 0; encephalitis lethargica, 6; dysentery, 105; ophthalmia neonatorum, 77. No case of cholera, plague or typhus fever was notified during the week.

The number of civilian and service sick in the Infectious Hospitals of the London County Council on July 21 was 1592. During the previous week the following cases were admitted: scarlet fever, 196; diphtheria, 40; measles 22; whooping-cough, 33.

Deaths.—In 126 great towns there were no deaths from scarlet fever, 2 (1) from enteric fevers, 1 (0) from measles, 6 (0) from whooping-cough, 12 (0) from diphtheria, 46 (6) from diarrhœa and enteritis under two years, and 5 (0) from influenza. The figures in parentheses are those for London itself.

Coventry reported 1 fatal case of enteric fever. Birmingham and Bristol each had 4 deaths from diarrhœa.

The number of stillbirths notified during the week was 195 (corresponding to a rate of 28 per thousand total births), including 18 in London.

Births, Marriages and Deaths

BIRTHS

BRITTON.—On July 29, in London, the wife of Dr. C. J. C. Britton—a son.

BROOKE.—On July 23, in London, the wife of Mr. Bryan N. Brooke, FRCS—a daughter.

CRICHTON.—On July 25, at Redhill, the wife of Dr. Crawford Crichton—a daughter.

CROWDEN.—On July 29, at Church Crookham, Hants, the wife of Lieut.-Colonel G. P. Crowden, RAMC—a daughter.

HUGGETT.—On July 28, to Prof. Esther Killick, MRCP, wife of Prof. A. St. G. Huggett—a daughter.

ORR.—On July 25, at Congleton, Cheshire, the wife of Lieut.-Colonel J. W. Orr, RAMC, of Rudyard, Staffs—a daughter.

TEASDALE.—On July 29, at Leeds, the wife of Surgeon Lieut.-Commander J. M. Teasdale, RNVR, of Retford, Notts—a daughter.

MARRIAGES

MULLER—MAYNE.—On July 24, at Greenwich, Andrej Muller, MD, second-lieutenant Czechoslovak Forces, to Mary Hyacinth Mayne, second officer WRNS.

RIVETT—STRATHIE.—On July 26, at Kilmacolm, Peter Alan Hastings Rivett, lieutenant RAMC, to Elspet Louise Strathie.

SCOTT—BRANFOOT.—On July 17, in London, Oliver Scott, MB, to Katherine Ogle Branfoot.

SITA—LUMSDEN.—On July 27, at Lyme Regis, Edward Gilbert Sita, surgeon-lieutenant RNVR, to Stella Pirie Lumsden.

DEATHS

COWEN.—On July 24, at Newbury, Thomas Philip Cowen, MD LOND., formerly medical superintendent of the Rainhill Mental Hospital, Liverpool, aged 75.

FRITH.—On July 30, at Hove, Baptist Gamble Frith, MB DUBL., aged 83.

GAMLEN.—On July 26, at North Cheriton, Somerset, Harold Ernest Gamlen, MB DURH., DPH, aged 72.

RENNIE.—On July 4, in India, William Benton Rennie, MC, MB ABERD., colonel late RAMC, aged 59.

SELBY.—On July 26, at Guildford, Edmond Wallace Selby, OBE, MD LOND., FRCS, of Leeds, retired divisional officer, Ministry of Health.

VAUGHAN-JACKSON.—On July 27, Percy Vaughan-Jackson, MRCS, surgeon captain RN, retd., of Sneyd, Berkhamsted, late Ballina, co. Mayo, aged 80.

WARD CLARKE.—On July 27, at Capel, Surrey, Harry Ward Clarke, MRCS, aged 79.

WHITEHOUSE.—On July 28, Sir Beckwith Whitehouse, MS LOND., CH M. HON. BIRM., FRCS, FRCOG, of Edgbaston.

Instances have occurred recently of local authorities advertising vacant medical posts in the journals without having first obtained the consent of the Minister of Health to filling the post, when this consent is necessary under circ. 2818. Candidates for appointments under local authorities would, therefore, be well advised to consult the Principal Regional Medical Officer in the region where they work before making an application.

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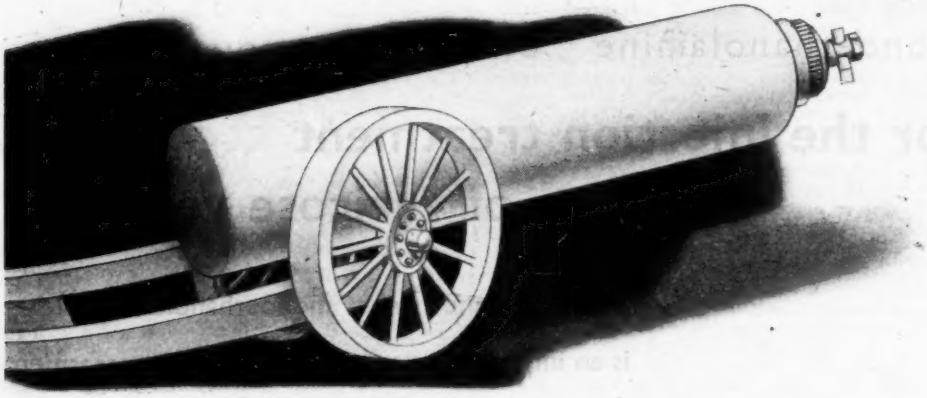

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Medical practitioners required for the position of TEMPORARY ASSISTANT MEDICAL OFFICER, Class I (B1), at NEW END HOSPITAL, Hampstead, N.W.3 (duties obstetrics and gynæcology). Salary £350 by £25 to £425 a year.

Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

TEMPORARY ASSISTANT MEDICAL OFFICERS, Class II (B2). Salary £250.

HACKNEY HOSPITAL, High-street, Homerton, E.9.—Mainly medical duties.

LAMBETH HOSPITAL, Brook-drive, S.E.11.—General duties, including work in radiotherapy department.

ST. ANDREW'S HOSPITAL, Devons-road, Bow, E.9.—General medical duties.

QUEEN MARY'S HOSPITAL FOR CHILDREN, Carshalton, Surrey.—Diseases of children.

R and W practitioners who now hold A posts may apply, when appointments will be limited to six months.

The above positions are with board, lodging, and washing. Married quarters are not available.

Application forms, obtainable from the MEDICAL OFFICER OF HEALTH (S.D.2), County Hall, S.E.1 (stamped addressed foolscap envelope necessary), returnable by 23rd August. Canvassing disqualifies.

South London Hospital for Women,

Clapham Common, S.W.4.

Applications are invited from registered medical Female practitioners for the undermentioned appointments, vacant 1st October:—

(1) GYNÆCOLOGICAL HOUSE SURGEON (B2). The appointment, which is recognised for M.R.C.O.G., is for a period of six months. Salary is at the rate of £100 per annum, with full residential emoluments. W practitioners who now hold A posts may apply.

(2) RESIDENT MEDICAL OFFICER (B1). Applicants should have held house appointments. Salary is at the rate of £200 per annum, with full residential emoluments. W practitioners who now hold B2 posts may apply.

Applications, stating age, nationality, qualifications with dates, and accompanied by copies of three recent testimonials, should be sent to the SECRETARY at the Hospital as soon as possible.

The Elizabeth Garrett Anderson

HOSPITAL, Euston-road, N.W.1

AT OSTER HOUSE E.M.S. HOSPITAL, St. Albans.

Applications are invited from registered medical Women practitioners for the appointment of HOUSE SURGEON (A), vacant 1st September, 1943. Appointment for six months. Salary £100 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply.

Applications, with two copies of each of three testimonials, should be sent to the SECRETARY of The Elizabeth Garrett Anderson Hospital by 18th August.

St. Bartholomew's Hospital, E.C.1.

Applications are invited from registered medical practitioners for the appointment of CHIEF ASSISTANT (B1) to the RADIOTHERAPEUTIC RESEARCH DEPARTMENT. It is desirable that candidates shall possess a diploma in medical radiology or the F.R.C.S. or M.R.C.P. Salary £500 per annum. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications, stating age, nationality, and qualifications, together with copies of not more than three testimonials, should be submitted not later than 16th August to—

C. CARUS-WILSON, Clerk to the Governors.

Miller General Hospital,

Greenwich High-road, S.E.10.

Applications are invited from registered medical practitioners, Male, for the appointment of RESIDENT OUT-PATIENT OFFICER (B1), vacant 23rd August, 1943. The post offers good facilities for practitioners studying for the higher examinations. Salary is at the rate of £250 per annum, with full residential emoluments. Suitably qualified R practitioners holding B2 appointments, also those holding B1 and rejected by the R.A.M.C., may apply.

Applications, giving full particulars, should be sent before 17th August, 1943, to: ERNEST E. MARKS, Secretary.

30th July, 1943.

HIS MAJESTY'S COLONIAL SERVICE

THE COLONIAL MEDICAL SERVICE

VACANCIES FOR MEDICAL OFFICERS

The maintenance of an efficient Colonial Medical Service constitutes a vital part of the national war effort and it is most important that the Service should be assured of an adequate supply of doctors.

The Secretary of State for the Colonies therefore invites applications from doctors possessing a medical qualification registrable in the United Kingdom who are British subjects and who are under thirty-five years of age.

Medical Officers are appointed in the first instance for general service. But there are ample opportunities for work in special branches of medicine and surgery, in public health and in medical research.

The normal salary scale is from £600 to between £1,000 and £1,120. There are large numbers of super-scale posts to which promotion is made on merit and which carry higher salaries.

Government quarters, in many cases free of rent, and first-class passages to and from the Colonies are provided, and an adequate pension scheme is in force.

Selected candidates are normally required to attend a course of instruction in Tropical Medicine and Hygiene either before proceeding overseas or during their first period of leave.

Further particulars, including the regulations governing admission to the Colonial Medical Service, may be obtained from the Director of Recruitment (Colonial Service), 2, Park-street, London, W.1.

Hampstead General Hospital,

Haverstock Hill, N.W.3.

Applications are invited from single medical Men or Women for following resident posts':—

JUNIOR MEDICAL OFFICER (B2) at MAIN HOSPITAL, Hampstead, N.W.3, embracing both surgical and medical work, vacant 1st October. Salary £133 6s. 8d. Tenable for six months.

CASUALTY MEDICAL OFFICER (B2) at OUT-PATIENT DEPARTMENT, Camden Town, N.W.1, vacant 1st September, or preferably 20th August. Salary £100 p.a. (tenable for six months), plus an allowance at £50 p.a. for duties in connexion with First-aid Post established there.

For both posts practitioners within three months of qualification and liable under National Service Acts may apply, when appointments will be temporarily down-graded to A. R and W practitioners who now hold A posts may apply.

Applications on the prescribed form, with copies of three testimonials, to be returned not later than 12th August.

KENNETH A. F. MILES, House Governor.

The Queen Elizabeth Hospital for CHILDREN, Glamis-road, Shadwell, E.1.

APPOINTMENT OF HOUSE PHYSICIAN (A).

Applications are invited from registered medical practitioners, Male or Female, for the above appointment, now vacant. The duties may include some attendance at the Hospital's country In-patient Department at Bayford, Herts. Appointment for six months. Salary at the rate of £150 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply.

Applications, accompanied by not more than three testimonials, must be made to the address given below on forms to be obtained from: CHARLES H. BESSELL, General Secretary.

The Queen Elizabeth Hospital for Children,
Hackney-road, E.2.

Hampstead General Hospital,

Haverstock Hill, N.W.3.

The Council of Management is prepared to receive applications for the office of TEMPORARY HONORARY SURGEON to the EAR, NOSE, AND THROAT DEPARTMENT, the office to be held for the duration of the war only. Candidates must be Fellows of the Royal College of Surgeons of England and ineligible for military service.

Applications, stating age, qualifications, and experience, with copies of three testimonials, must reach the undersigned by 23rd August, from whom full particulars of the appointment may be obtained.

By Order of the Council,
KENNETH A. F. MILES, House Governor.

Tilbury Hospital, Essex.

Applications are invited from registered British practitioners for the appointment of HOUSE OFFICER (A). Salary is at the rate of £160 p.a., with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply, when appointment will be for a period of six months.

Applications, stating age, qualifications with dates, accompanied by copies of three recent testimonials, to be sent to the undersigned, marked "Tilbury." F. A. LYON, Secretary.

Seamen's Hospital Society, Greenwich, S.E.10.

Wembley Hospital, Middlesex.

(118 Beds.)

Applications are invited from registered medical practitioners (Male) for the appointment of a JUNIOR RESIDENT MEDICAL OFFICER (A), vacant immediately. The appointment will be for six months. Salary is at the rate of £175 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply.

Applications should reach the undersigned as soon as possible.

30th July, 1943. P. E. WINDO, Secretary.

East Ham Memorial Hospital,

Shrewsbury-road, E.7.

Applications are invited from registered medical practitioners for the appointment of HOUSE SURGEON AND CASUALTY OFFICER (A), vacant 15th August. Salary is at the rate of £120 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply, when the appointment will be for six months.

Applications, stating full particulars, accompanied by copies of three testimonials, should be forwarded immediately to—

REGINALD PERRY, Secretary-Superintendent.

Bolingbroke Hospital,

Wandsworth Common, S.W.11.

Applications are invited from registered medical practitioners for the following appointments:—

TEMPORARY PATHOLOGIST.—The appointment will be for the period of the war, and the successful candidate will be required to attend at the Hospital on one or two days a week. A payment will be made at the rate of two and a half guineas per attendance.

TEMPORARY ANÆSTHETIST.—The appointment will be for the period of the war, and the successful candidate will be required to undertake anæsthetic duties on one or more half-days per week. There is an honorarium of thirty guineas a year attaching to the post.

Applications, stating age, qualifications, &c., accompanied by copies of three testimonials, to be sent on or before the 18th August to—

W. S. RANDOLPH BISS, Secretary-Superintendent.

County Council of Essex and Corporation OF CHINGFORD.

APPOINTMENT OF TEMPORARY ASSISTANT COUNTY MEDICAL OFFICER AND MEDICAL OFFICER OF HEALTH.

Applications are invited for the above appointment from persons not eligible for military service.

The minimum commencing salary as Assistant County Medical Officer will be at the rate of £400 a year, and the minimum commencing salary as Medical Officer of Health will be at the rate of £400 a year. The total salary of the person appointed will rise, subject to satisfactory service, by annual increments of £25 to a maximum of £900 a year. An allowance at the rate of £78 a year in respect of travelling will also be made to the successful candidate. The amounts of any increments in salary and the travelling allowance will be shared equally by the respective authorities.

The successful applicant will, in addition to his other duties, be required to undertake Civil Defence duties in the Borough of Chingford.

Applicants must be duly qualified medical Men, with experience in public health duties, and hold a Diploma of Public Health.

Applications must be made on the prescribed form, obtainable from the Clerk of the County Council, accompanied by copies of not more than three recent testimonials, which will not be returned, and should be delivered at the County Hall, Chelmsford, not later than 28th August, 1943.

JOHN E. LIGHTBURN, Clerk of the County Council.
GEO. E. MALLEY, Town Clerk.

County Hall, Chelmsford, 29th July, 1943.

City of Manchester.

WITHINGTON HOSPITAL. (1150 Beds.)

LOCUM TENENS RESIDENT OBSTETRICAL OFFICER (B1).

Applications are invited for this post from registered medical practitioners, for a period of two or three weeks' duty at any time during August or September, 1943.

Fee £10 10s. weekly, with full board and residence in addition.

Apply to Dr. GREENWOOD, Medical Superintendent, Withington Hospital, West Didsbury, Manchester, 20.

Resident Medical Officer (B2)

YORK MATERNITY HOSPITAL.

Applications are invited from registered medical practitioners (Female) for the appointment of RESIDENT MEDICAL OFFICER (B2). The duties of the successful applicant will consist of maternity and child welfare work in connexion with the York Maternity Hospital and the Child Welfare Clinics; she will be expected to perform other duties as may be prescribed by the Medical Officer of Health. There is a Senior Medical Officer in charge.

The appointment will be for six months and is subject to the Council's Sick Allowance Regulations.

The salary will be at the rate of £200 per annum, together with emoluments (board-residence at the Hospital, valued at £150 per annum). A war bonus (at present £13) is also paid. W practitioners who now hold A posts may apply.

Applications, stating age, nationality, qualifications with dates, experience and details of previous appointments, together with copies of three recent testimonials, should be sent to—

P. R. MCNAUGHT, M.D., Medical Officer of Health.
50, Bootham, York.

Stone Rural District Council.

The Stone Rural District Council invite applications from duly qualified medical Men, including practitioners of not less than three years' standing in their profession, for the post of Part-time MEDICAL OFFICER OF HEALTH to the Council.

The successful applicant will be required to carry out the duties outlined in the Public Health Act, 1936, any regulations made thereunder, or under any other statutory enactment or order, particulars of which can be obtained from the undersigned.

The salary will be at the rate of £175 per annum, and travelling expenses will be at the rate of £40 per annum. The appointment will be subject to one month's notice on either side.

Applications, accompanied by copies of not more than two recent testimonials, must be received by the Clerk to the Council, R.D.C. Offices, Stone, Staffs, not later than 10th August, 1943.

IVAN G. GASKIN, Clerk to the Council.
Rural District Council Offices, Stone, Staffs, 27th July, 1943.

Surrey County Council Hospital Service.

PART-TIME DIRECTOR OF PHYSICAL MEDICINE at ST. HELIER COUNTY HOSPITAL, CARSHALTON (862 Beds) and KINGSTON COUNTY HOSPITAL (500 Beds).

Applications for the above appointment from doctors of high standing in the specialty of Physical Medicine should be sent to the County Medical Officer, County Hall, Kingston-on-Thames, by 31st August, 1943. Salary £1200 p.a.

The Director of Physical Medicine will be required to devote a minimum of twenty-four hours per week to the Council's service (eighteen hours at St. Helier Hospital and six hours at Kingston Hospital).

Applications will, however, be considered from candidates who can devote a substantial period to the duties at one or other of these hospitals, but who cannot give twenty-four hours per week to the Council's service. If a smaller number of hours per week is arranged the salary will be at a pro rata figure. The physiotherapy at St. Helier Hospital is a new department, including gymnasium and a wide range of treatment rooms.

DUDLEY AUKLAND, Clerk of the Council.

Nottingham City Hospital.

Applications are invited from registered medical practitioners (Male) for the appointment of RESIDENT JUNIOR HOUSE SURGEON (A). The appointment will be limited to six months. Salary at the rate of £250 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply.

Applications, stating age, qualifications with dates, and nationality, should be accompanied by copies of three testimonials and sent to: J. E. RICHARDS, Town Clerk.
Guildhall, Nottingham.

Southport General Infirmary.

(150 Beds.)

Applications are invited from registered medical practitioners (Male, single) for the appointment of HOUSE PHYSICIAN (A), commencing 1st September. The salary is at the rate of £150 per annum, with full residential emoluments. R practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of recent testimonials, should be addressed to the SUPERINTENDENT, Infirmary, Southport.

Doncaster Royal Infirmary.

Applications are invited from medical practitioners (Male or Female) for the appointment of HOUSE SURGEON (A). The appointment will be for six months. Salary £175 per annum, with full residential emoluments. This large industrial area offers excellent opportunities for gaining experience. Practitioners within three months of qualification and liable under the National Service Acts may also apply.

Applications, accompanied by not more than three testimonials, to be sent immediately to—

R. LANCASTER, Secretary-Superintendent.

County Borough of Bury.

Applications are invited from registered medical practitioners for the position of Whole-time DEPUTY MEDICAL OFFICER OF HEALTH (Temporary). Duties will include those at a Tuberculosis Dispensary, in the diagnosis and treatment of venereal disease cases, and in school medical work. Preference will be given to candidates possessing experience necessary to carry out the above-mentioned duties. The salary will be at the rate of £750 per annum, rising to £850 per annum by annual increments of £25. The appointment will be subject to six weeks' notice on either side, and may be subject also to the provisions of the Local Government Superannuation Act, 1937, for which purpose the successful candidate will be required to pass a medical examination.

Applications, stating age, qualifications, experience, liability for military service, medical fitness, and position as regards deferment, and accompanied by copies of not more than three recent testimonials, should be forwarded to the undersigned not later than 13th August, 1943. There is no special form of application. H. D. A. ROBERTSON, Town Clerk.
Municipal Offices, Bank-street, Bury, 26th July, 1943.

Royal Hospital for Sick Children,

GLASGOW.

Applications are invited from registered medical practitioners for the appointment of RESIDENT SURGICAL OFFICER (B1) in the Royal Hospital for Sick Children, vacant shortly. Applicants should have held house appointments and have had surgical experience. Preference will be given to candidates holding a higher qualification in surgery. Salary is at the rate of £400. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply, but must first have obtained sanction of the Scottish Central Medical War Committee to their application.

Applications, stating age, nationality, qualifications with dates, experience, and details of previous appointments, and accompanied by copies of three recent testimonials, should be sent not later than fourteen days after the date of this Journal to: HANNAH B. ROBERTSON, Acting Secretary.
86, St. Vincent-street, Glasgow, 27th July, 1943.

Gravesend and North Kent Hospital.

Applications are invited from registered medical practitioners, Male, for the appointment of HOUSE SURGEON (A), now vacant. Salary is at the rate of £175 p.a., with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

Applications should be addressed to the SECRETARY-SUPERINTENDENT.

Preston Royal Infirmary.

(404 Normal Beds—9 Residents.)

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE SURGEON (A), vacant 31st August. Salary at the rate of £150 per annum, with the usual residential emoluments. Duties under Consulting Surgeon. This post is recognised as approved experience for the F.R.C.S. examination. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

Applications should be sent to: JOHN GIBSON, Superintendent.
Royal Infirmary Preston.

St. Margaret's Hospital, Epping.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE OFFICER (B2). The salary is at the rate of £200 p.a., with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months; otherwise it will not exceed one year.

Applications should be made in writing to the COUNTY MEDICAL OFFICER, County Hall, Chelmsford, and should include applicant's full name, age, nationality, qualifications, and details of previous posts (if any), and whether liable to service under the National Service Acts.

Royal Cornwall Infirmary, Truro.

(330 Beds—5 Residential.)

Applications are invited from registered practitioners (Male or Female) for the appointment of HOUSE SURGEON (B2) to the OPHTHALMIC and EAR, NOSE, AND THROAT DEPARTMENTS with some general surgical duties, now vacant. Salary is at the rate of £200 per annum, with full residential emoluments. Practitioners holding A posts (males must be rejected by the R.A.M.C.) may also apply, when appointment is limited to six months.

Applications should be addressed to the SECRETARY.

De-la-Pole Hospital

(FOR NERVOUS AND MENTAL DISORDERS),
WILLERBY, Near HULL.

Required immediately TEMPORARY MEDICAL OFFICER (B1) (Male) to replace one called up. Salary £8 8s. per week, plus full residential emoluments. Applications from male R practitioners holding B2 posts, also those holding B1 and rejected by the R.A.M.C., may apply.

Apply MEDICAL SUPERINTENDENT.

Hull Royal Infirmary.

Applications are invited from registered medical practitioners for the following posts, vacant October, at the PARENT HOSPITAL and SUTTON BRANCH HOSPITAL :—

SENIOR HOUSE SURGEON (B1). Salary £225 per annum. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

HOUSE SURGEON (B2) and HOUSE PHYSICIAN (B2) (two posts). Salary £200 per annum. R and W practitioners who now hold A posts may apply, when appointments will be limited to six months.

Two CASUALTY OFFICERS (A). Salary £200 per annum. Practitioners within three months of qualification and liable under the National Service Acts may apply, when appointments will be for a period of six months.

Each of the above posts carries full residential emoluments.

Applications should be addressed to—

R. J. CARLESS, House Governor.

University of Durham.

KING'S COLLEGE, NEWCASTLE UPON TYNE.
DEPARTMENT OF PATHOLOGY.

Applications are invited from registered medical practitioners of either sex for the following full-time posts :—

Two LECTURERS in the Department of Pathology of the Medical School, King's College and the Royal Victoria Infirmary, Newcastle upon Tyne.

Previous experience in pathological anatomy and hæmatology essential. Each appointment is a war emergency one. The salary of each post is at the rate of £600 per annum. The persons appointed will be required to commence duties as soon as possible.

Applications, accompanied by the names of not more than three referees, should be submitted on or before Friday, 20th August, 1943, to the PROFESSOR OF PATHOLOGY, Medical School, King's College, Newcastle upon Tyne, 2, from whom further particulars may be obtained.

University of Durham.

The MEDICAL SCHOOL, KING'S COLLEGE, AND ROYAL VICTORIA INFIRMARY, NEWCASTLE UPON TYNE.

Applications are invited for the position of Whole-time FIRST ASSISTANT in the DEPARTMENT OF MEDICINE. The appointment, the duties of which are to assist in teaching and research, will be for one year in the first instance, renewable annually for a total period of three years. Salary £450–£600, according to qualifications and experience.

Applications, including three recent testimonials or the names of three persons willing to act as references, should be sent to the undersigned, from whom further particulars may be obtained, not later than Saturday, 14th August.

G. R. HANSON, Registrar.

University of Birmingham.

FACULTY OF MEDICINE.

Applications are invited for the post of ASSISTANT LECTURER AND DEMONSTRATOR in the PHYSIOLOGY DEPARTMENT. Stipend at the rate of £300 per annum. Duties to begin 1st October, 1943.

Four copies of application, with testimonials, must be sent on or before 18th August to the undersigned, from whom further particulars may be obtained. C. G. BURTON, Secretary.

Brookwood Mental Hospital, Knaphill,

WOKING, SURREY.

Applications are invited from medical practitioners, including R and W practitioners holding B2 posts, for the post of TEMPORARY ASSISTANT MEDICAL OFFICER (B1), which will become vacant at the above Hospital about the middle of September. Salary £450; rising to £550 per annum, with full residential emoluments. R practitioners holding B1 posts and rejected by the R.A.M.C. may also apply.

Applications in writing, accompanied by three recent testimonials, should be sent to the MEDICAL SUPERINTENDENT as soon as possible.

Bedford County Hospital.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE SURGEON (B2), vacant 1st September. The salary is at the rate of £190 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months.

Bedford. HORACE R. NEATE, Secretary.

Royal Cornwall Infirmary, Truro.

(330 Beds—5 Residents.)

Applications are invited from registered practitioners (Male or Female) for the appointment of HOUSE SURGEON (B2) to the GENERAL SURGICAL AND GYNÆCOLOGICAL DEPARTMENTS, now vacant. Salary is at the rate of £200 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months.

Applications should be addressed to the SECRETARY.

17th July, 1943.

Newark Town and District Hospital.

(70 Normal Beds.)

Applications are invited from registered medical practitioners, Male and Female, for the following appointments, vacant 8th September :—

HOUSE SURGEON (B2). Salary is at the rate of £200 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months.

HOUSE SURGEON (A). Salary is at the rate of £175 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

Applications to : B. C. DION, Secretary-Superintendent.

Westmorland County Hospital,

KENDAL. (82 Beds.)

Applications are invited from registered medical practitioners for the appointment of HOUSE SURGEON (B2), now vacant. Salary £300 per annum, with board, residence, and laundry. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months ; otherwise may be extended.

Applications, stating age, qualifications with dates, nationality, present post, and accompanied by copies of three recent testimonials, should be sent without delay to J. M. SOMERVELL, Hon. Secretary.

Huddersfield Royal Infirmary.

(321 Beds.)

Applications are invited for the combined appointment of RESIDENT ANÆSTHETIST AND ASSISTANT CASUALTY OFFICER (A), duties to commence immediately. Salary at the rate of £150, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply, when appointment will be for a period of six months.

Applications should be sent as soon as possible to—

H. J. JOHNSON, General Superintendent and Secretary.

Huddersfield Royal Infirmary.

(321 Beds.)

Applications are invited for the combined appointment of HOUSE PHYSICIAN AND HOUSE SURGEON (B2) to the EAR, NOSE, THROAT, AND EYE DEPARTMENT. Duties to commence immediately. Salary at the rate of £187 10s., with full residential emoluments. R and W practitioners who now hold A posts may apply. The appointment will be limited to six months.

Applications should be sent as soon as possible to—

H. J. JOHNSON, General Superintendent and Secretary.

Huddersfield Royal Infirmary.

(321 Beds.)

CASUALTY OFFICER (B2) required to commence duty on 31st August, 1943. Salary at the rate of £200, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months.

Applications should be sent as soon as possible to—

H. J. JOHNSON, General Superintendent and Secretary.

Berks and Bucks Joint Sanatorium,

Peppard Common, HENLEY-ON-THAMES, OXON.

Applications are invited from registered medical practitioners of either sex for the appointment of TEMPORARY SENIOR ASSISTANT MEDICAL OFFICER. Applicants should have had previous experience in the treatment of pulmonary tuberculosis.

The selected candidate will be required to undergo a medical examination and to contribute to the Joint Committee's Superannuation Scheme. Salary is at the rate of £450, with annual increments of £25 to a maximum of £525, together with full residential emoluments, valued for superannuation purposes at £150 per annum.

No form is provided and candidates should submit their own applications, stating age and nationality, with copies of not more than three testimonials, to the undersigned, from whom further details are available, not later than 21st August, 1943. HARLEY STEVENS, Medical Superintendent.

31st July, 1943.

City and County of Bristol.

DEPARTMENT OF PUBLIC HEALTH.

HAM GREEN HOSPITAL AND SANATORIUM.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of ASSISTANT RESIDENT MEDICAL OFFICER (B2) at Ham Green Hospital. Salary is at the rate of £200 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months ; otherwise it will be for a period of one year.

Application forms may be obtained from the undersigned, to whom they must be returned, accompanied by copies of not more than three recent testimonials, not later than the 21st August, 1943. R. H. PARRY, Medical Officer of Health.

Kenwith Lodge, Westbury Park, Bristol, 6.

Northumberland County Council.

MATERNITY UNIT, THOMAS TAYLOR HOMES, STANNINGTON.

Applications are invited for the appointment of RESIDENT OBSTETRIC OFFICER (B2) at the above Maternity Unit, which is a recently constructed hospital of 20 Beds with modern equipment. Applicants should have had previous resident experience in a maternity hospital, and preference will be given to candidates who have some knowledge of maternity and child welfare work. The officer appointed may be required to undertake attendance at a Child Welfare Centre and Antenatal Clinic in addition to the duties of Resident Obstetric Officer. Salary is at the rate of £350 per annum (including war bonus), plus board, lodging, and laundry. The appointment is subject to medical examination, is for a period of one year, and is terminable at any time by one month's notice on either side. Practitioners holding A posts may apply, when appointment will be limited to six months.

Applications, stating age, nationality, qualifications, and experience, and accompanied by copies of three recent testimonials, should be submitted as soon as possible to the undersigned, from whom further particulars may be obtained.

Dr. JOHN B. TILLEY, County Medical Officer.

County Hall, Newcastle/Tyne, 1.

Northumberland County Council.

HEXHAM EMERGENCY HOSPITAL.
(Regional Orthopædic Centre. 640 Beds.)

HOUSE SURGEONS (A).

Applications for the above posts are invited from registered medical practitioners, Male or Female. Salary is at the rate of £120 per annum, with full residential emoluments. The Hospital offers excellent training and experience in orthopædic surgery. Practitioners within three months of qualification and liable under the National Service Acts may apply, when appointment will be for a period of six months; otherwise it will be for a period of one year.

Applications, stating age, qualifications with dates and nationality, and accompanied by copies of recent testimonials, should be sent immediately to the undersigned.

J. B. TILLEY,
County Medical Officer.

County Hall, Newcastle upon Tyne, 1,

Borough of Hove.

TEMPORARY ASSISTANT MEDICAL OFFICER OF HEALTH AND ASSISTANT SCHOOL MEDICAL OFFICER.

Applications from suitably qualified Men or Women, preferably not liable for military service, are invited for the above appointment. Salary £650 per annum, together with a car allowance of £50 per annum, determinable on either side by three months' notice. The post is subject to the Local Government Superannuation Act, 1937, and to the successful candidate, who will be precluded from engaging in private practice, passing a medical examination. The duties include work in connexion with the Public Health and School Medical Services, and also Civil Defence. Preference will be given to candidates having a knowledge of infectious diseases, including tuberculosis, and possessing the D.P.H. The consent of the Ministry of Health has been given to this appointment.

Applications, accompanied by full particulars of the candidate's qualifications and liability for military service, together with copies of three recent testimonials, should be sent to the Medical Officer of Health, Town Hall Annexe, Third-avenue, Hove, on forms to be obtained from him and returned as soon as possible.

23rd July, 1943. W. JERMYN HARRISON, Town Clerk.

General Hospital, Nottingham.

(585 Beds.)

Applications are invited from registered medical practitioners for the appointment of RESIDENT ORTHOPÆDIC AND FRACTURE OFFICER (B1), vacant shortly. Applicants should have had previous experience in Fracture and Orthopædic work. The Orthopædic Department serves a large industrial district and the post offers exceptional experience in traumatic surgery. The appointment will be for a period of one year in the first instance. Salary is at the rate of £300 per annum, with full residential emoluments. Suitably qualified R practitioners holding B2 appointments, also those holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications, stating age, nationality, qualifications, with three copy testimonials, to be forwarded as soon as possible to—

H. M. STANLEY, House Governor and Secretary.

Royal Albert Edward Infirmary and DISPENSARY, WIGAN. (Normally 189 Beds.)

Applications are invited from registered medical practitioners (Male) for the appointment of HOUSE SURGEON (A), now vacant. Salary is at the rate of £150 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply, when appointment will be for a period of six months; otherwise may be extended for a further period.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three recent testimonials, should be sent as soon as possible to—

A. STANLEY BRUNT, General Superintendent and Secretary.

County Borough of St. Helens.

Applications are invited for the post of TEMPORARY ASSISTANT MEDICAL OFFICER OF HEALTH (Female).

The duties will be mainly in connexion with the Maternity and Child Welfare and School Medical Services, together with such other duties as the Medical Officer of Health may from time to time direct. Candidates must have special experience in midwifery and in the diseases of children.

The salary will be at the rate of £600 per annum, plus travelling expenses, rising by annual increments of £25 to a maximum of £700 per annum, plus a temporary war cost-of-living bonus at present at the rate of £24 per annum.

The appointment is subject to the provisions of the Local Government Superannuation Act, 1937, and to the successful candidate passing the necessary medical examination.

The approval of the Ministry of Health has been obtained for the appointment, and candidates should submit with their applications full information as to their liability for military service, medical fitness, and position as regards deferment.

Forms of application may be obtained from the Medical Officer of Health, Town Hall, St. Helens, and completed applications, accompanied by copies of not more than three recent testimonials, should reach him not later than the 14th August, 1943. FRANK HAUXWELL, Medical Officer of Health.

Town Hall, St. Helens, 16th July, 1943.

Bucks County Council.

PUBLIC HEALTH DEPARTMENT.

HOUSE PHYSICIAN (B2), EMERGENCY MATERNITY HOME.

Applications are invited from registered Women practitioners for the post of House Physician (B2) at the Emergency Maternity Home, Shardeloes, Amersham. The appointment will be for a period of six months. The home of 48 Beds is set up under the Government Evacuation Scheme and receives all types of maternity cases. The successful candidate will work under the supervision of the Resident Obstetric Consultant. The salary is at the rate of £200 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply.

Form of application may be obtained from the COUNTY MEDICAL OFFICER, County Offices, Aylesbury, and should be returned to him not later than 16th August, 1943, accompanied by copies of not more than three recent testimonials.

County Offices, Aylesbury, 26th July, 1943.

Huntingdonshire County Council.

PUBLIC HEALTH DEPARTMENT.

Applications are invited from registered medical practitioners (Female) for the post of RESIDENT MEDICAL OFFICER (B1) at PAXTON PARK EMERGENCY MATERNITY HOME in the County of Huntingdonshire. Candidates must have had previous midwifery experience. The salary will be at the rate of £200 per annum, with full board, lodging, and laundry. Suitably qualified W practitioners holding B2 or B1 appointments may apply. The post is limited to a period of one year.

Applications, stating age, nationality, qualifications, and experience, and accompanied by copies of not more than two recent testimonials, should be sent at once to—

N. H. HARRISON, County Medical Officer.

County Offices, Gazeley House, Huntingdon.

Rochdale Infirmary, Lancs.

The Board of Management invite applications from registered medical practitioners (Male and Female) for the appointment of SECOND HOUSE SURGEON (A), vacant shortly. Salary is at the rate of £150 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

The successful candidate will be required to be a member of a medical defence society. W. WYNNE, Secretary.

Newcastle upon Tyne Eye Hospital.

Applications are invited for the position of HOUSE SURGEON (A) (Male or Female), at a commencing salary of £200 to £300 per annum (according to previous experience), all found. The staff consists of three House Surgeons and the Hospital is recognised for the purposes of the D.O.M.S. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

Applications, with testimonials, should be addressed to the SECRETARY, Eye Hospital, St. Mary's-place, Newcastle upon Tyne.

Royal South Hants and Southampton HOSPITAL, SOUTHAMPTON. (255 Beds.)

Applications are invited from registered medical practitioners, Male and Female, for the appointment of CASUALTY OFFICER (A), vacant 20th August, 1943. The appointment will be for a period of six months. Salary is at the rate of £175 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply.

Applications, stating age, qualifications with dates, nationality, and present post, and accompanied by copies of three recent testimonials, should be sent immediately to—

EDWARD L. WIRGMAN, House Governor and Secretary.

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Leicester Royal Infirmary.

PRELIMINARY NOTICE.

VACANCIES, 1st October, 1943.

Applications are invited from registered medical practitioners, Male and Female, for following posts:

RESIDENT SURGICAL OFFICER (B1). Salary £400 per annum.

GYNÆCOLOGICAL AND OBSTETRIC HOUSE SURGEON (B2). Minimum Salary £125 per annum.

TWO HOUSE SURGEONS (A). Salary £125 per annum.

RESIDENT ANÆSTHETIST (B2). Salary £150 per annum.

SENIOR CASUALTY OFFICER (B1). Salary £200 per annum. A suitable candidate will be asked to deputise for Resident Surgical Officer.

JUNIOR CASUALTY OFFICER AND EAR, NOSE AND THROAT HOUSE SURGEON (A). Salary £125 per annum. 6 months' appointments. All with full residential emoluments.

For the B1 posts: Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

For the B2 posts: R and W practitioners who now hold A posts may apply.

For the A posts: Practitioners within three months of qualification and liable under the National Service Acts may also apply.

H. T. PLOWMAN, House Governor and Secretary.

31st July, 1943.

County of Warwick.

WARWICK HOSPITAL.

Applications are invited from registered medical practitioners (Male and Female) for the appointment of ORTHOPÆDIC REGISTRAR (B1), now vacant. Applicants should have had previous experience in orthopædic and fracture work. The Warwick Hospital is a Fracture A Hospital with 150 fracture and orthopædic beds. Salary £600 per annum, together with the usual residential emoluments. If accommodation cannot be provided at the hospital a non-resident allowance at the rate of £100 per annum will be made. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications should be made on forms which may be obtained from the PUBLIC ASSISTANCE OFFICER, Shire Hall, Warwick, and should be returned to him on completion not later than the 25th August, 1943. L. EDGAR STEPHENS, Clerk of the Council.

Shire Hall, Warwick.

Worthing Hospital,

Lyndhurst-road, WORTHING.

Applications are invited from registered medical practitioners for the appointment of RESIDENT SURGICAL OFFICER (B1), Male. Applicants should have held house appointments and had surgical experience. Preference will be given to candidates holding diploma of F.R.C.S. Salary is at the rate of £350 per annum. Suitably qualified R practitioners holding B2 appointments, also those holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications, stating age, nationality, qualifications with dates, experience, and details of previous appointments, should be accompanied by copies of recent testimonials.

A. V. OAKTON, House Governor.

The Prince of Wales's Hospital,

Greenbank-road, PLYMOUTH.

Applications are invited from registered medical practitioners for the appointment of RESIDENT SURGICAL OFFICER (B1), vacant 24th September. Applicants should have held house appointments and had surgical experience. Preference will be given to candidates holding diploma of F.R.C.S. Salary is at the rate of £252 per annum. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply. ARTHUR R. CASH, General Superintendent.

30th July, 1943.

Thurrock E.M.S. and Infectious Diseases

HOSPITAL. (172 Beds.)

Applications are invited from registered medical practitioners for the appointment of HOUSE OFFICER (A), Male or Female. Salary at the rate of £120 per annum, with board, lodging, and laundry. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months; otherwise not exceeding one year.

Applications, stating age and qualifications, to be addressed to the undersigned, to arrive not later than 21st August, 1943.

A. E. POOLE, Clerk to the Council.

Council Offices, Whitehall-lane, Grays, 29th July, 1943.

Royal Cornwall Infirmary, Truro.

(330 Beds—5 Residential.)

Applications are invited from registered practitioners (Male or Female) for the appointment of ORTHOPÆDIC AND CASUALTY HOUSE SURGEON (B2), now vacant. Salary is at the rate of £200 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months.

Applications should be addressed to the SECRETARY.

July 28th, 1943.

Newport Mental Hospital, Caerleon, Mon.

Applications are invited from registered medical practitioners for the post of TEMPORARY ASSISTANT MEDICAL OFFICER (B1) at the above Hospital. Salary £500 per annum, rising by annual increments of £25 to £600, plus cost-of-living bonus of £16 per annum, together with full residential emoluments. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners now holding B1 appointments and rejected by R.A.M.C., may apply. The appointment will be subject to termination by one month's notice in writing.

S. M. T. BURPITT,

Town Clerk and Clerk to the Visiting Committee.

Town Hall, Newport, Mon.

East Surrey Hospital, Redhill, Surrey.

Applications are invited from registered medical practitioners (Female), including practitioners within three months of qualification who are liable to service under the National Service Acts for the appointment of HOUSE SURGEON (A), vacant 1st September. The appointment will be for a period of six months. Salary at the rate of £100 per annum, with full residential emoluments.

Applications should be addressed to: E. C. AYLING, Secretary

University of Otago, Dunedin,

NEW ZEALAND.

Applications are invited for the following positions:—

PROFESSOR OF PHYSIOLOGY (salary £1500–£2000).

SENIOR LECTURER ANATOMY (salary £750–£900 or £1000).

SENIOR LECTURER PHYSIOLOGY (salary £750–£900 or £1000).

All salaries in New Zealand currency.

For full particulars apply to the HIGH COMMISSIONER FOR NEW ZEALAND, 415, Strand, London, W.C.2, by whom applications will be received up to the 31st August, 1943.

Wanted at once, Locum Tenent, for about two months, in Yorks, semi-rural district. Full-time assistant already in practice will be available. Permanency possible. Reply, sending two recent references, to: Address, No. 297, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Doctors, Male and Female, required for duration Locums, Locums, and Assistantships, in Yorkshire, Lancashire, Wales, &c. Good salaries paid. Vacancies for Hospital Locums and Ships' Surgeons.—Write A. SHAW, Medical Agent, Premier Buildings, 88, Church-street, Liverpool, 1.

Industrial Medical Officer (Male) wanted for large Engineering Works near Glasgow about to develop a Medical Service. Commencing salary depends on qualifications and experience, but will be around £1000 p.a. Excellent scope under first-class conditions.—Apply, with copies of three recent testimonials to Address, No. 306, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Long period Locum required for Shropshire country. Salary £650 per annum, all found.—Write A. SHAW, Medical Agent, Premier Buildings, 88, Church-street, Liverpool, 1.

Assistant required, out-door, Male or Female, for Practice on the Durham, Yorkshire border. Salary £750 per annum, including car. Many other Assistantships and Locums.—Write A. SHAW, Medical Agent, Premier Buildings, 88, Church-street, Liverpool, 1.

Wanted, for good-class Practice within 25 miles of London, ASSISTANT with view to Partnership. Should be well qualified and university graduate preferred.—Write, Address, No. 301, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Intelligent and reliable Woman with first-class experience requires post as SECRETARY-RECEPTIONIST with a doctor in London. Well qualified in shorthand, typewriting, and book-keeping.—Address, No. 305, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Medical Practices and Partnerships for disposal; also Dental Practices. All classes of Insurance transacted.—Write A. SHAW, Medical Agent, Premier Buildings, 88, Church-street, Liverpool, 1.

Gunnersbury Park, London, W.5.— Desirable modern Freehold Residence for Sale. Would suit professional man, more particularly medical practitioner. Open position, direct route to town; lounge, dining, and 4 bedrooms, half-tiled kitchen, tiled bathroom, and downstair cloakroom, &c.; electricity (power) throughout; garage and good-sized front and rear gardens. Immediate possession. Price £2250. Vendor might consider letting furnished for time being. Apply by letter only—KENNEDY, GENESE & CO., Solicitors, 49, Queen Victoria-street, E.C.4.

Doctors' Cars for Hire. Special rates for self drive. Telephone: FULham 7781.

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3 In subacute combined degeneration Anahæmin is specially indicated; by its use the danger of permanent damage to the nervous system through inadequate treatment is avoided.

4 A minimum content of therapeutically inert reaction-producing protein substances is attained as a result of the special method of preparation of Anahæmin.

5 Anahæmin alone is sufficient to produce complete recovery in all cases of pernicious anæmia and to correct all the remediable neurological signs and symptoms of subacute combined degeneration. No additional treatment is required.

Details of dosage and other relevant information will be gladly supplied on request.

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